IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY

DEPOMED, INC., Plaintiff, v. ACTAVIS ELIZABETH LLC, et al., Defendants.	:	C.A. No. 3:12-cv-01358-JAP-TJB REDACTED

DEFENDANTS ACTAVIS ELIZABETH LLC'S AND ACTAVIS LLC'S FINDINGS OF FACT AND CONCLUSIONS OF LAW

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	DTX 36	Actavis Elizabeth LLC, Product Development Report: Gabapentin Once-Daily Tablets, 300 mg and 600 mg (2011) (*confidential*).
	DTX 39	Am. Pharmacists Ass'n, TABLETING SPECIFICATION MANUAL 56, Fig. 25 (7th ed. 2006)
	DTX 88	Depomed Inc., Quarterly Review: Gralise Marketing Update (July 24, 2012) (*confidential*).
Hwang	DTX 222	Sung-Joo Hwang, et al., Gastric Retentive Drug-Delivery Systems, Critical Reviews, 15 CRITICAL REVIEWS IN THERAPEUTIC DRUG CARRIER SYS. 243, 243–84 (1998).
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WO '755	DTX 230	Int'l Patent Publ'n No. WO 93/18755 (filed Mar. 17, 1993).
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Neurontin Label	DTX 291	Pfizer, Neurontin® Product Label (1999) (FDA approved labeling Oct. 12, 2000).
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Rowbotham	DTX 313	Michael Rowbotham et al., Gabapentin for the treatment of Postherpetic Neuralgia: A Randomized Controlled Trial, 280 J. AM. MED. ASS'N 1837, 1837-42 (1998).
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'475 Patent	DTX 397	U.S. Patent No. 6,340,475 (filed March 29, 1999).
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'475 Patent	DTX 397	U.S. Patent No. 6,340,475 (filed March 29, 1999).
'962 Patent	JTX 1	U.S. Patent No. 6,488,962 (filed June 20, 2000).
'280 Patent	JTX 2	U.S. Patent No. 6,635,280 (filed Nov. 6, 2001).
'927 Patent	JTX 3	U.S. Patent No. 7,438,927 (filed Oct. 25, 2002).
'989 Patent	JTX 4	U.S. Patent No. 7,731,989 (filed Sept. 26, 2008).
'756 Patent	JTX 5	U.S. Patent No. 8,192,756 (filed May 19, 2011).
'332 Patent	JTX 6	U.S. Patent No. 8,252,332 (filed March 29, 2010).
'992 Patent	JTX 7	U.S. Patent No. 8,333,992 (filed July 27, 2012).
	JTX 9	U.S. Patent No. 6,488,962 Certified File History (filed June 10, 2000).
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	PHYJTX 2	Physical sample of the Actavis 600 mg ANDA Product specified in ANDA No. 203611 (*confidential*).
	PTX 14	Actavis Elizabeth LLC, Original ANDA # 203611, Gabapentin Once-Daily Tablets, 300 mg and 600 mg - Section 2.3 Introduction to the Quality Overall Summary (*confidential*).
	PTX 44	Actavis Purchase Requisition (Excel Native).
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	PTX 238	Actavis Gabapentin Tablets Described in ANDA No. 20393 - Quantitative Tablet Swelling Study, *In Vitro* Dissolution and Qualitative Tablet Imaging Study of Gabapentin Tablets, Report No. R120924B (*confidential*).
Timmermans	PTX 245	Jacques Timmermans & André Moës, The Cutoff Size for Gastric Emptying of Dosage Forms, 82 J. PHARMACEUTICAL SCI. 854 (1993).
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Stewart	PTX 271	Barbara H. Stewart et al., A Saturable Transport Mechanism in the Intestinal Absorption of Gabapentin Is the Underlying Cause of the Lack of Proportionality Between Increasing Dose and Drug Levels in Plasma, 10 PHARMACEUTICAL RES. 276, 276-81 (1993).
	PTX 277	XenoPort Press Release, PR Newswire, Preclinical Studies of XenoPort's Gabapentin Demonstrate (Nov. 22, 2002).
	PTX 311	Depomed, Inc., Depomed Financial Management Report (July 2013) (*confidential*).
	PTX 332	Daniel T. Mallon, Excerpts of Lab Notebook regarding Gabapentin Tablets (2012).
Stevenson	PTX 500	Cheryl Miles Stevenson, et al., Colonic Absorption of Antiepileptic Agents, 38 EPILEPSIA 63, 63-67 (1997).

INTRODUCTION

1. The evidence in this case has made one principle clear: without an inventor, there can be no invention. Although Depomed presented several witnesses over the course of trial, it did not present testimony from the named inventors of the Patents-In-Suit – those people who are perhaps best-equipped to describe any so-called inventive process that lead to the patents at issue. Instead, the deposition testimony of a single named inventor, Dr. Sui Yuen Eddie Hou, was presented by Actavis. Although his explanation was short, he did testify as to how Depomed arrived at the Patents-In-Suit – Depomed simply followed the breadcrumbs laid out in the prior art, placing the known drug gabapentin into Depomed's known dosage form (which had been published in Depomed's own WO '107), motivated by the known characteristics of gabapentin that make it a suitable drug for a gastric-retained dosage form. The product is intended for a known therapeutic use of gabapentin – the treatment of post-herpetic neuralgia. Thus, the reason why Depomed did not present the inventors at trial is because the Patents-In-Suit contain no new invention.

2. If there ever was any innovation by Depomed, it occurred in 1997, when Depomed first filed the patent application that led to WO '107. WO '107 was published to the world in 1998, and discloses a swellable, gastric-retained dosage form that can be used for a variety of highly soluble drugs. WO '107 also gave rise to the claims in U.S. Patent No. 6,340,475, which is no longer being asserted by Depomed against Actavis in this case, and which has already given Depomed nearly 20 years of patent protection on its swellable dosage form technology. The evidence shows that after filing WO '107, Depomed simply added incremental embellishments to an existing product, which to those of ordinary skill in the art were no more than obvious variations on an established theme. As to the asserted claims of the

'280 Patent, Depomed's embellishment resulted in indefinite claims, the scope of which cannot be determined by one of ordinary skill in the art, let alone the public.

3. This case concerns three categories of patents owned by Depomed: (i) the platform patent, which claims swellable, gastric-retained oral dosage forms (the '280 Patent); (ii) the oval patent, which covers a specific shape and particular dimensions of a gastric-retained dosage form (the '962 Patent); and (iii) the patents disclosing gabapentin-containing dosage forms (the '927, '989, '756, '332 and '992 Patents). The below chart contains a high-level summary of the issues as to the asserted claims of each patent-in-suit:

Patent	Claims	Expires	Issues
The Platform Patent			
'280	1, 12, 14, 45	Sept. 19, 2016	***Invalidity:*** The asserted claims are indefinite. ***Noninfringement:*** Actavis' ANDA Products do not swell to a size exceeding the pyloric diameter in the fed mode.
The Oval Patent (only asserted against Actavis' 600 mg Product)			
'962	5, 8, 10, 13[1]	June 20, 2020	***Invalidity:*** The asserted claims are obvious over WO '107. ***Noninfringement:*** Actavis' 600 mg ANDA Products are not oval. (Not asserted against Actavis' 300 mg product)
The Gabapentin Patents			
'927	18, 25, 26, 34, 61, 62[2]	Feb. 26, 2024	***Invalidity:*** The asserted claims are obvious over WO '107 in view of Rowbotham. ***Noninfringement:*** (1) Actavis' ANDA Products do not swell to increase their size to promote gastric retention in the stomach; and (2) Actavis does not indirectly infringe the asserted method claims.
'989	10[3]	Oct. 25, 2022	***Invalidity:*** The asserted claims are obvious over WO '107 in view of Rowbotham. ***Noninfringement:*** Actavis' ANDA Products do not swell to increase their size to promote gastric retention in the stomach.
'756	1, 2, 5, 6, 7, 11	Oct. 25, 2022	***Invalidity:*** The asserted claims are obvious over WO '107 in view of Rowbotham. ***Noninfringement:*** (1) Actavis' ANDA Products do not swell to increase their size to promote gastric retention in the stomach; and (2) Actavis does not indirectly infringe the asserted method claims.
'332	1, 6, 17, 22, 24[4]	Oct. 25, 2022	***Invalidity:*** The asserted claims are obvious over either WO '107 or WO '128, in view of Rowbotham. ***Noninfringement:*** Actavis does not indirectly infringe the asserted method claims.
'992	1, 5, 22[5]	Oct. 25, 2022	***Invalidity:*** The asserted claims are obvious over either WO '107 or WO '128, in view of Rowbotham. ***Noninfringement:*** Actavis does not indirectly infringe the asserted method claims.

[1] Claims 5, 8, 10 and 13 of the '962 Patent depend directly or indirectly from claim 1, which is not asserted by Depomed.

[2] Claims 18, 25, 26 and 61 of the '927 Patent depend from claim 17, which is not asserted by Depomed. Claims 34 and 62 depend from claim 33, which is also not asserted.

[3] Claim 10 of the '989 Patent depends from claim 1, which is not asserted by Depomed.

[4] Claim 6 of the '332 Patent depends directly or indirectly from claims 1, 4 and 5. Claims 4 and 5 are not asserted by Depomed. Claim 17 depends from claim 12, which is also not asserted.

[5] Claim 5 of the '992 Patent depends from claim 4, which is not asserted.

4. By the priority date of the Patents-In-Suit, all elements of the asserted claims of the Gabapentin Patents and the '962 Patent were known in the art to those of ordinary skill. In fact, Depomed's own WO '107 clearly disclosed the claimed gastric-retained dosage form. Further, Depomed does not dispute that a motivation to make a controlled release of gabapentin existed and that the only feasible way to do so was a gastric-retained dosage form in view of gabapentin's absorption characteristics. The only remaining issue, then, is whether persons of ordinary skill in the art at the time of the invention would have had a reasonable expectation of success in doing so. The evidence shows that they would have. And the Patents-In-Suit themselves state that the WO '107 formulation is suitable for use with gabapentin, undermining the positions currently taken by Depomed's experts before this Court. Depomed certainly does not deserve 20 more years of patent protection each time it makes a small, obvious change to its dosage form or each time it places another drug into its formulation.

FINDINGS OF FACT

I. PROCEDURAL HISTORY

5. Plaintiff, Depomed, Inc. ("Depomed"), filed the present action for patent infringement on March 2, 2012, against defendants Actavis LLC and Actavis Elizabeth LLC (collectively, "Actavis"), among others, alleging that Actavis' filing of ANDA No. 203611 infringed U.S. Patent Nos. 6,340,475 ("the '475 Patent"), 6,488,962 ("the '962 Patent"), 6,635,280 ("the '280 Patent"), 6,723,340 ("the '340 Patent"), 7,438,927 ("the '927 Patent") and 7,731,989 ("the '989 Patent") under 35 U.S.C. § 271(e)(2)(A) and that Actavis' commercial manufacture, use, offer for sale, or sale of the products set forth in ANDA No. 203611 (the "ANDA Products") within the United Sates, or importation of the ANDA Products into the United States during the term of the '475, '962, '280, '340, '927 and '989 Patents would infringe the asserted patent claims under 35 U.S.C. § 271(a), (b) and/or (c). (Stip. Fact ¶¶ 6, 23, 24.)

6. Depomed subsequently amended its complaint to allege infringement of U.S. Patent Nos. 8,192,756 ("the '756 Patent"), 8,252,332 ("the '332 Patent") and 8,333,992 ("the '992 Patent"). (Stip. Fact ¶¶ 28, 31, 34.)

7. Depomed holds New Drug Application ("NDA") No. 22-544 for tablets that contain 300 mg and 600 mg of the active ingredient gabapentin for once-daily administration. (Stip. Fact ¶¶ 2, 3.) These products are sold under the brand name "Gralise," and are approved for the treatment of post-herpetic neuralgia. (Stip. Fact ¶ 3.) The "Approved Drug Products with Therapeutic Equivalence Evaluations" (the "Orange Book") lists the '475, '280, '340, '962, '927, '989, '756, '332 and '992 Patents for Gralise. (See Stip. Fact ¶¶ 15, 17, 19, 21.)

8. Actavis filed counterclaims asserting that the '475, '280, '340, '962, '927, '989, '756, '332 and '992 Patents are invalid and/or not infringed. (Stip. Fact ¶¶ 26, 29, 32, 35.)

9. Depomed subsequently withdrew its claims of infringement for the '475 and '340 Patents. (Stip. Fact ¶ 39.)

10. Depomed also stipulated that Actavis' 300 mg ANDA Product does not infringe the '962 Patent. (Stip. Fact ¶ 41.) Thus, with respect to the '962 Patent, Depomed only alleges infringement with respect to Actavis' 600 mg ANDA Product.

11. The United States Food and Drug Administration ("FDA") has tentatively approved Actavis' ANDA.

12. The Court held a seven day bench trial on the issue of infringement and invalidity of the '280, '962, '927, '989, '756, '332 and '992 Patents (the "Patents-In-Suit") from May 12 to May 20, 2014.

II. BACKGROUND

13. At the time the Patents-In-Suit were filed, gabapentin was not a new drug. As named inventor Dr. Hou testified, Depomed did not discover gabapentin. (5/14/2014 Tr. 547:24-548:1.) Instead, gabapentin was conceived of and synthesized in the early 1970s at Goedecke, A.G., in Germany, which was part of Warner-Lambert at the time, as testified to by Dr. Gidal. (Stip. Fact ¶ 117; 5/16/2014 Tr. 857:3-9.) Warner-Lambert obtained FDA approval and commercialized an immediate release formulation of gabapentin as under the brand name Neurontin® in December 1993 – nearly a decade before the priority dates of the Patents-In-Suit. (Stip. Fact ¶ 119; 5/15/2014 Tr. 686:1-5.) Further, Dr. Hou admitted that Depomed did not develop gabapentin to treat postherpetic neuralgia. (5/14/2014 Tr. 548:3-5.) As several of the experts from both sides explained, gabapentin and its relevant properties, including its therapeutic applications, were well known in the prior art. (5/16/2014 Tr. 857:3-9.) For instance, as Dr. Flanagan explained, gabapentin was known in the prior art to be an effective treatment of neuropathic pain. (5/14/2014 Tr. 559:4-560:5, 622:17-623:3; DTX 313

at GRALISE_JDG_00000452.) Through gabapentin's use to treat neuropathic pain, Dr. Gidal testified that its pharmacokinetic parameters were also known in the prior art. (5/16/2014 Tr. 858:7-11.)

14. Gabapentin was also known in the prior art to have some unique absorption properties. It is uncontested that gabapentin was known to be highly water soluble. (See 5/14/2014 Tr. 558:5-559:3; DTX 267 at GRALISE_JDG_00000126; 5/15/2014 Tr. 703:19-24; DTX 291 at GRALISE_JDG_00000152; 5/13/2014 Tr. 263:16-17.) As Dr. Flanagan explained, gabapentin was also known to have a narrow window of absorption in the upper gastrointestinal tract and to be absorbed via a saturable transporter. (5/14/2014 Tr. 560:6-561:9, 564:22-565:1; PTX 500 at GRALISE_JDG_00000601, GRALISE_JDG_00000603; DTX 267 at GRALISE_JDG_00000127.) These properties would have made gabapentin inappropriate for a traditional controlled release formulation. (5/15/2014 Tr. 769:24-770:3, 702:4-16, 713:22-714:17.) Drs. Flanagan and Felton agreed that a person of ordinary skill in the art, however, would have known that these properties made gabapentin ideal for a gastric retained, controlled release dosage form. (5/15/2014 Tr. 637:2-6; 5/19/2014 Tr. 964:15-965:16.)

15. Depomed had been developing gastric retained, controlled release dosage forms for highly soluble drugs since the 1990s. International Patent Publication No. WO 98/55107 A1 ("Depomed's WO '107"), authored by Depomed employees, discloses "Gastric-Retentive Oral Drug Dosage Forms for Controlled Release of Highly Soluble Drugs." (DTX 234 at GRALISE_JDG_00000841-871.) As described by Drs. Flanagan and Mayersohn, Depomed's WO '107, like other prior art, describes a gastric retained dosage form intended for highly soluble drugs that uses swellable polymers to increase their size in the stomach in the fed mode in order to slowly release a highly soluble drug by diffusion into the stomach and to the upper

digestive tract. (5/14/2014 Tr. 556:22-557:8; 5/15/2014 Tr. 699:15-700:3.) Although gabapentin was not one of the drugs listed in Depomed's WO '107, Depomed admitted that gabapentin's known absorption characteristics made it a good candidate for a gastric retained, controlled release dosage form – in fact, it was the only type of dosage form considered. (5/14/2014 Tr. 548:11-17.)

16. Depomed's WO '107 later matured with some additional information added to the '475 Patent's specification. (5/15/2014 Tr. 685:11-14; see also DTX 234 at GRALISE_JDG_00000841 (showing the priority application of U.S. Application No. 08/870,509); DTX 397 at GRALISE_JDG_00001235 (showing the '475 Patent is a continuation-in-part of application No. 08/870,509).) In fact, claim 1 of Depomed's WO '107 is nearly identical to claim 1 of the '475 Patent, as seen below:

Claim 1 of Depomed's WO '107	**Claim 1 of Depomed's '475 Patent**
A controlled release oral drug dosage form for releasing a drug whose solubility in water is such that one part of said drug dissolves in less than ten parts by weight of water,	A controlled release oral drug dosage form for releasing a drug whose solubility in water is greater than one part by weight of said drug in ten parts by weight of water,
said dosage form comprising a solid polymeric matrix in which said drug is dispersed at a weight ratio of drug to polymer of about 80:20 or less,	said dosage form comprising a solid polymeric matrix with said drug dispersed therein at a weight ratio of drug to polymer of from about 15:85 to about 80:20,
said polymeric matrix being one that swells to at least about twice its volume upon imbibition of water,	said polymeric matrix being one that swells upon imbibition of water thereby attaining a size large enough to promote retention in the stomach during said fed mode,
that releases said drug into gastric fluid by the dissolution and diffusion of said drug out of said matrix by said gastric fluid,	that releases said drug into gastric fluid by the dissolution and diffusion of said drug out of said matrix by said gastric fluid,
that upon immersion in gastric fluid retains at least about 40% of said drug one hour after such immersion and releases substantially all of said drug within about eight hours after such immersion, and	that upon immersion in gastric fluid retains at least about 40% of said drug one hour after such immersion and releases substantially all of said drug within about eight hours after such immersion, and

Claim 1 of Depomed's WO '107	Claim 1 of Depomed's '475 Patent
that remains substantially intact until all of said drug is released.	that remains substantially intact until all of said drug is released.

(DTX 234 at GRALISE_JDG_00000858; DTX 397 at col. 17, ll. 45-59.)

17. Dr. Flanagan testified that Depomed simply took the prior art gastric retentive dosage form, as disclosed in Depomed's WO '107, and incorporated "a known drug with known properties and known therapeutic uses." (5/14/2014 Tr. 553:6-7.) Notably, Depomed did not call a single inventor during the trial to describe an "Eureka" moment – that is because there is not one. The alleged inventions set forth in the Patents-In-Suit were developed by Depomed doing nothing more than following the teachings of the prior art and claiming the resulting product.

18. Depomed is already enjoying patent protection for its alleged innovation through, for example, the '475 Patent, a continuation-in-part of Depomed's WO '107, as testified by Dr. Flanagan. (5/15/2014 Tr. 685:11-14.) The '475 Patent does not expire until September 19, 2016. (DTX 397 at GRALISE_JDG_00001235.) Depomed originally asserted the '475 Patent against Actavis, but later voluntarily dropped from its complaint. (Stip. Fact ¶¶ 6, 23, 24, 39.) The '475 Patent, allegedly covering Depomed's general gastric-retained dosage form technology, is the predecessor to the '280 Patent, and one of the patents on which the '962 Patent is an alleged improvement. Through the '475 Patent, Depomed will obtain the benefit of a full 20-year term of patent protection for its gastric retention technology.

III. THE PATENTS-IN-SUIT

A. Priority Dates

19. Depomed stated that the priority date of the asserted claims of the '280 Patent is June 6, 1997. (D.I. 213-2 (Ex. 1) (Depomed's Infringement Contentions (Oct. 8, 2012)), p. 6; D.I. 221 at 2.)

20. Depomed stated that the priority date of the asserted claims of the '962 Patent is June 20, 2000. (D.I. 213-2 (Ex. 1), p. 6; D.I. 221 at 2.)

21. Depomed has stated that the priority date for the asserted claims of the '927, '989, '756, '332 and '992 Patents (the "Gabapentin Patents") is October 25, 2001. (Depomed's Amended Infringement Contentions (June 28, 2013), p. 4; D.I. 213-2 (Ex. 1), p. 6; D.I. 221, p. 2.)

B. U.S. Patent No. 6,635,280 – The Platform Patent

22. The '280 Patent, entitled "Extending the Duration of Drug Release Within the Stomach During the Fed Mode," issued on October 21, 2003, to Depomed from a patent application filed on November 6, 2001, as a continuation from United States Patent No. 6,340,475 ("the '475 Patent"). (Stip. Fact ¶¶ 8, 50.) Depomed asserted claims 1, 12, 14 and 45 of the '280 Patent. (Stip. Fact ¶ 51.)

1. Background

23. The '280 Patent purports to provide an improvement over prior art gastric retained dosage forms. (5/19/2014 Tr. 1025:13-16.) When the application for the '280 Patent was first filed with the United States Patent and Trademark Office ("PTO"), claim 1 did not require that the dosage form exceed the pyloric diameter in the fed mode when swollen. (JTX 10 at DEPOACT0002492.) On December 18, 2002 the PTO mailed a non-final rejection of all of the claims in the application for the '280 Patent for statutory double patenting over the

'475 Patent. (Id. at DEPOACT0002545-48.) In response to this rejection, Depomed amended the pending claims to, among other things, include the limitation "is of a size exceeding the pyloric diameter in the fed mode." (Id. at DEPOACT0002551-52.) Depomed also argued that the amendment overcame the PTO's rejection of the claims. (Id. at DEPOACT0002576.)

2. The Asserted Claims

24. Claim 1 of the '280 Patent is directed to:

> A controlled release oral drug dosage form for releasing a drug whose solubility in water is greater than one part by weight of said drug in ten parts by weight of water, said dosage form comprising one or more polymers forming a solid polymeric matrix with said drug incorporated therein at a weight ratio of drug to polymer of from 15:85 to 80:20, said dosage form being one that when swollen in a dimensionally unrestricted manner as a result of imbibition of water is of a size exceeding the pyloric diameter in the fed mode to promote retention in the stomach during said fed mode, that releases said drug into gastric fluid by the dissolution and diffusion of said drug out of said matrix by said gastric fluid, that upon immersion in gastric fluid retains at least about 40% of said drug one hour after such immersion and releases substantially all of said drug after such immersion, and that remains substantially intact until substantially all of said drug is released.

(Stip. Fact ¶ 53, JTX 2 at col. 17, ll. 45-61.)

25. The remaining asserted claims depend from claim 1, and add the following limitations: (a) the "polymeric matrix is formed of poly(ethylene oxide) at a molecular weight in the range of about 5,000,000 to about 8,000,000" (claim 12); (b) the "polymeric matrix upon immersion in gastric fluid retains at least about 60% of said drug one hour after such immersion" (claim 14); and (c) the "dosage form releases substantially all of said drug within about ten hours after immersion in gastric fluid" (claim 45). (Stip. Fact ¶¶ 52, 59-61; JTX 2 at col. 18, ll. 29-31, 37-39; col. 26, ll. 25-26.)

C. U.S. Patent No. 6,488,962 – The Oval Patent

26. The '962 Patent, entitled "Tablet Shapes To Enhance Gastric Retention of Swellable Controlled-Release Oral Dosage Forms," issued on December 3, 2002, to Depomed from a patent application filed on June 20, 2000. (Stip. Fact ¶¶ 7, 40.) This patent is not asserted against Actavis' 300mg ANDA Product – Depomed asserted claims 5, 8, 10 and 13 of the '962 Patent only against Actavis' 600 mg ANDA Product. (Stip. Fact ¶ 41.)

1. Background

27. The '962 Patent purports to provide an improvement over prior art gastric retained dosage forms. (5/19/2014 Tr. 938:2-19.) The specification explains that, although dosage forms that swell to sizes that will prolong the residence time in the stomach were known in the art (including Depomed's WO '107), the tablet could still be expelled from the stomach depending on the tablet's orientation in the stomach. (JTX 1 at col. 2. l. 52 - col. 3, l. 5.) More specifically, the specification of the '962 Patent states:

> Even with swelling, a certain proportion of particles can pass through the pylorus regardless of whether the subject is in the fed mode or the fasting mode, if the particles become oriented when in the vicinity of the pylorus such that their longest dimension is in alignment with the pyloric axis. This is particularly true of tablets or caplets (cylindrical tablets with rounded ends) that are elongated in shape to facilitate swallowing. When dosage forms such as these swell due to imbibition of water, one dimension may achieve a length great enough to exceed the pyloric opening while the others may be significantly smaller. The dosage form will thus be retained in the stomach only if the form is oriented with the long dimension transverse to the pyloric opening. Accordingly, for a certain percentage of the administered units of these swellable forms, prolonged retention in the stomach is not achieved and the beneficial effect of the swelling is lost. There is thus only a limited assurance that the swelling will result in gastric retention of the dosage form.

(Id. at col. 3, ll.1-19.)

28. The specification explains that "by using a solid water-swellable dosage form of a particular shape, the proportion of these dosage forms that escapes through the pylorus due to a fortuitous orientation at the pylorus can be reduced or eliminated entirely while still having a dosage form that is easily swallowed." (Id. at col. 3, ll. 23-27.) The specification goes on to state in the summary of the invention that "[t]he shape that achieves this result is a non-circular and non-spherical shape which, when projected onto a planar surface, has two orthogonal axes of different lengths . . . ." (Id. at col. 3, ll. 27-30.)

29. With respect to the types of shapes contemplated, the specification states that:

> the dosage forms of this invention . . . may vary in shape. Some of the possible shapes are oval, triangle, almond, peanut, 'bow tie,' parallelogram, trapezoidal, pentagonal, and hexagonal, provided (as stated above) that the largest planar projection of the shape has at least two orthogonal dimensions, one being larger than the other. Preferred shapes are oval and parallelogram (notably diamond-shaped, i.e., a quadrilateral in which opposing sides are parallel and adjacent sides are not at right angles). In certain embodiments, the edges or corners of these shapes, particularly those of the parallelogram, are slightly rounded. Particularly preferred shapes are those that have three (orthogonal) planes of symmetry to aid in swallowing.

(Id. at col. 4, ll. 7-21.) One of ordinary skill in the art would understand each of the possible shapes to be distinct shapes. (5/14/2014 Tr. 466:24-467:17, 468:17-19, 469:2-7.)

30. When the application for the '962 Patent was first filed with the PTO, the claim did not require that the dosage form have a particular shape. In response to an Office Action rejecting the then-pending claims, however, Depomed amended the claims to include the limitation that "wherein said matrix has a shape which when projected onto a plane, is either an oval or a parallelogram." (JTX 1 at col. 11, ll.24-26, DEPOACT0002365; 5/14/2014 Tr. 469:24-470:8.)

2. The Asserted Claims

31. Claim 1 of the '962 Patent is directed to:

> A controlled release oral drug dosage form for releasing a drug into at least a portion of a region defined by the stomach and the upper gastrointestinal tract, said dosage form consisting essentially of a solid monolithic matrix with said drug contained therein, said matrix being non-circular in shape and having first and second orthogonal axes of unequal length, said matrix being one that swells in an unrestricted manner along both such axes upon imbibition of water, the longer such axis having a maximum length of 3.0 cm when said matrix is unswollen, and the shorter such axis achieving a minimum length of 1.2 cm within one hour of immersion of said dosage form in water and wherein said matrix has a shape which when projected onto a plane, is either an oval or a parallelogram.

(Stip. Fact ¶ 432; JTX 1 at col. 11, ll. 14-26.)

32. Claims 5, 8, and 10 depend from claim 1, and add the following limitations: (a) the dosage form where the "shorter axis has a length of 0.7 cm to 1.5 cm when said matrix is unswollen" (claim 5); (b) the dosage form where the "longer axis has a maximum length of 2.5 cm when said matrix is unswollen" (claim 8); and (c) where the "matrix is a water-swellable polymer" (claim 10). (Stip. Fact ¶¶ 42, 46-48; JTX 1 at col. 11, ll. 38-39, 47-48 and 53-54.)

33. Claim 13 depends from claim 10, and adds the following limitation: the dosage form where the "water-swellable polymer is a member selected from the group consisting of poly(ethylene oxide), hydroxypropylmethyl cellulose, and hydroxyethyl cellulose" (claim 13). (Stip. Fact ¶¶ 42, 49; JTX 1 at col. 12, ll. 2-5.)

D. The Gabapentin Patents

1. Background

34. The Gabapentin Patents arise from the same patent application, and they have patent specifications that are identical in all material respects.

35. The specification of the Gabapentin Patents explains that gabapentin was available in various tablet and capsule dosage forms with recommended daily dosing of 900 mg to 1800 mg total daily dose in three divided dosages. (JTX 3 at col 1, ll.13-17.) The specification explains that because gabapentin's absorption is saturable carrier-mediated, the oral bioavailability of gabapentin decreases with increasing dose. (Id. at col. 1, ll. 17-24.) Furthermore, the specification describes publications from other researchers that found that the site of absorption of gabapentin was in the duodenum.[6] (Id. at col. 1, ll. 25-31.)

36. The Gabapentin Patents' specification explains that the alleged invention is nothing more than treating a disease state by administering gabapentin in a once- or twice-daily gastric retained dosage form. (JTX 3 at col. 2, ll. 14-16.) The specification states that a number of gastric retained dosage forms were known in the art. In particular, the specification states:

> There are several drug delivery systems that are suitable for use in delivering gabapentin in the method of the invention as they are particularly tailored to be gastric-retained dosages, such as the swellable bilayer described by Franz, et al., U.S. Pat. No. 5,232,704; the multi-layer tablet with a band described by Wong, et al., U.S. Pat. No. 6,120,803; the membrane sac and gas generating agent described in Sinnreich, U.S. Pat. No. 4,996,058; the swellable hydrophilic polymer system described in Shell, U.S. Pat. No. 5,972,389 and Shell, et al., WO9855107; all of which are incorporated herein by reference.

(Id. at col. 5, ll. 52-62.)

37. The Gabapentin Patents' specification further explains that gastric retained dosage forms "of particular interest" contain certain polymers that were known in the art to have a high swelling capacity in water, such as polyethylene oxide, hydroxyethylcellulose and hydroxypropylmethylcellulose. (Id. at col. 5, l. 63 – col. 6, l. 1.)

[6] The duodenum is the uppermost part of the small intestine directly below the stomach. (5/12/2014 Tr. 152:11-153:1.)

38. The Examples in the Gabapentin Patents state that pharmacokinetic profiles of three gastric retained gabapentin formulations were compared to Neurontin-brand immediate-release gabapentin formulations. Based on these data, in Example 4, the specification states that the gastric retained formulations "demonstrate sustained release with a lower maximum plasma concentration and a larger value for the time of maximum concentration compared to the immediate release capsules without loss in the bioavailability as measured by the plasma $AUC_{inf.}$" (Id. at col. 11, ll. 28-32.)

2. U.S. Patent No. 7,438,927

39. The '927 Patent, entitled "Methods of Treatment Using a Gastric Retained Gabapentin Dosage," issued on October 21, 2008, to Depomed from a patent application filed on October 25, 2002. (Stip. Fact ¶¶ 9, 62.) Depomed asserted claims 18, 25, 26, 34, 61 and 62 of the '927 Patent. (Stip. Fact ¶ 63.) Each of the asserted claims depend from either of two independent claims – claim 17 or claim 33 – neither of which is asserted in this litigation.

40. Claim 17 of the '927 Patent is representative and is directed to:

> A method of treating neuropathic pain in a mammal comprising administering a therapeutically effective amount of a daily dosage of about 100 mg to about 4800 mg of gabapentin or a pharmaceutically acceptable salt thereof, dispersed in a gastric retained dosage form to the mammal in which a fed mode has been induced, wherein the dosage form comprises a single polymer matrix comprising at least one swellable hydrophilic polymer that swells in a dimensionally unrestrained manner by imbibing water to increase its size to promote gastric retention of the dosage form in the stomach of the mammal, and wherein upon contact with water, gabapentin is released by diffusion from the dosage form over a period of at least five hours and at least 40 wt% of the gabapentin is retained in the dosage form one hour after administration.

(Stip. Fact ¶ 65; JTX 3 at col. 12, ll. 38-51.)

41. Claim 33 of the '927 Patent differs from claim 17, only with respect to the preamble. Instead of reciting a "method of treating neuropathic pain" as in claim 17, claim 33 is instead directed to:

> A method of administering a therapeutically effective amount of a daily dosage of about 100 mg to about 4800 mg of gabapentin to a mammal, comprising administering gabapentin or a pharmaceutically acceptable salt thereof, dispersed in a gastric retained dosage form to the mammal in which a fed mode has been induced and wherein the dosage form comprises a single polymer matrix comprising at least one swellable hydrophilic polymer that swells in a dimensionally unrestrained manner by imbibing water to increase its size to promote gastric retention of the dosage form in the stomach of the mammal, and wherein upon contact with water, gabapentin is released by diffusion from the dosage form over a period of at least five hours and at least 40 wt % of the gabapentin is retained in the dosage form one hour after administration.

(Stip. Fact ¶ 70; JTX 3 at col. 12, l. 38; col. 13, ll. 25-39.)

42. The remaining asserted claims depend from either claim 17 or 33, and add the following limitations: (a) administering the dosage form once-daily (claims 18, 34); (b) the gastric-retained dosage form release gabapentin to the stomach, duodenum and small intestine (claim 25); (c) the gastric retained dosage form provides administration of at least 85 wt % of the gabapentin to be delivered over a period of 5-12 hours (claim 26); and (d) the mammal to which the dosage form is administered is a human (claims 61 and 62). (Stip. Fact ¶¶ 66, 67, 68, 69, 71, 72; JTX 3 at col. 12, ll. 52-53; col. 13, ll. 1-6, 40-41; col. 14, ll. 50-53.)

3. U.S. Patent No. 7,731,989

43. The '989 Patent, entitled "Gastric Retained Gabapentin Dosage Form," issued on June 8, 2010, to Depomed from a patent application filed on September 26, 2008, as a continuation of the '927 Patent. (Stip. Fact ¶¶ 10, 73.) Depomed asserted claim 10 of the '989 Patent. (Stip. Fact ¶ 74.)

44. The only asserted claim of the '989 Patent depends from claim 1. Claim 1 of the '989 Patent is directed to:

> A dosage form, comprising between about 100 mg to about 4800 mg of gabapentin or pharmaceutically acceptable salt thereof, dispersed in a single polymer matrix comprising at least one swellable hydrophilic polymer that swells unrestrained dimensionally by imbibing water to increase its size to promote gastric retention of the dosage form in a stomach in a fed mode, wherein upon contact with water, gabapentin is released by diffusion from the dosage form over a period of at least five hours and at least 40 wt % of the gabapentin is retained in the dosage form 1 hour after administration.

(Stip. Fact ¶¶ 75-76; JTX 4 at col. 12, ll. 9-18.)

45. Claim 10 of the '989 Patent contains the additional requirement that "the gabapentin has a bioavailability greater than or equal to 80% of an equal dose of gabapentin in an immediate release dosage form." (Stip. Fact ¶ 77; JTX 4 at col. 12, ll. 37-39.)

4. U.S. Patent No. 8,192,756

46. The '756 Patent, entitled "Gastric Retained Gabapentin Dosage Form," issued on June 8, 2010, to Depomed from a patent application filed on May 19, 2011, as a continuation of the '927 Patent. (Stip. Fact ¶¶ 11, 78.) Depomed asserted claims 1, 2, 5, 6, 7 and 11 of the '756 Patent. (Stip. Fact ¶ 79.)

47. Claim 1 of the '756 Patent is directed to:

> A dosage form, comprising:
>
> comprising from 100 mg to 4800 mg of therapeutically effective amount of gabapentin or pharmaceutically acceptable salt thereof, dispersed in a single matrix
>
> wherein the matrix comprises at least one swellable hydrophilic polymer that swells unrestrained dimensionally by imbibing water to increase its size to promote gastric retention of the dosage form in the stomach in a fed mode,
>
> wherein upon once-daily or twice-daily ingestion of the dosage form gabapentin is released from the matrix over a period of at least five

> hours wherein at least 40 wt% of the gabapentin is retained in the matrix one hour after administration, and
>
> wherein the gabapentin is released at a rate sufficient to achieve a lower maximum plasma concentration (C_{max}) compared to an equal dose of gabapentin provided by an immediate release dosage form, and without loss in bioavailability as measured by the area under the curve ($AUC_{infinity}$) as compared to the bioavailability which is achieved from an immediate release dosage form comprising the same dose of gabapentin.

(Stip. Fact ¶ 81; JTX 5 at col. 12, l. 50 – col. 13, l. 3.)

48. Claim 6 of the '756 Patent is identical to claim 1, except that it describes a method of treating a condition using the gabapentin-containing dosage form:

> A method of treating a condition responsive to a therapeutic dose of gabapentin, comprising:
>
> orally administering once-daily or twice daily a dosage form comprising between about 100 mg to about 4800 mg of gabapentin or pharmaceutically acceptable salt thereof, dispersed in a single matrix,
>
> wherein the matrix comprises at least one swellable hydrophilic polymer that swells unrestrained dimensionally by imbibing water to increase its size to promote gastric retention of the dosage form in the stomach in a fed mode,
>
> wherein upon once-daily or twice daily ingestion of the dosage form gabapentin is released from the matrix over a period of at least five hours wherein at least 40 wt% of the gabapentin is retained in the matrix one hour after administration, and
>
> whereby the dosage form releases gabapentin at a rate sufficient to achieve a lower maximum plasma concentration (C_{max}) compared to an equal dose of gabapentin provided by an immediate release dosage form, and without loss in bioavailability as measured by the area under the curve ($AUC_{infinity}$) as compared to the bioavailability which is achieved from an immediate release dosage form comprising the same dose of gabapentin.

(Stip. Fact ¶ 85; JTX 5 at col. 13, ll. 14-38.)

49. The remaining asserted claims depend from claim 1, and add the following limitations: (a) the time to reach maximum plasma concentration is longer relative to the time to

reach maximum plasma concentration from an immediate release dosage form comprising the dose of gabapentin (claims 2 and 7); (b) the dosage form comprises a dose of gabapentin of between about 300-600 mg (claim 5); and (c) the condition treated in the method is neuropathic pain (claim 11). (Stip. Fact ¶¶ 83, 84, 86, 87; JTX 5 at col. 13, ll. 4-7, 12-13; col. 14, ll. 1-4, 10-11.)

5. U.S. Patent No. 8,252,332

50. The '332 Patent, entitled "Gastric Retained Gabapentin Dosage Form," issued on August 28, 2012, to Depomed from a patent application filed on March 29, 2010, as a continuation of the '927 Patent. (Stip. Fact ¶¶ 12, 88.) Depomed asserted claims 1, 6, 17, 22 and 24 of the '332 Patent. (Stip. Fact ¶ 89.)

51. Claim 1 of the '332 Patent is directed to:

> A dosage form, comprising a matrix comprising gabapentin, wherein upon ingestion of the dosage form gabapentin is released from the matrix into the upper gastrointestinal tract over about 5-12 hours at a rate sufficient to achieve a lower maximum plasma concentration than that provided by an immediate release dosage form comprising an equal amount of gabapentin, and bioavailability of gabapentin is at least 80% of that provided by the immediate release dosage form comprising an equal amount of gabapentin as measured by the area under the plasma concentration-time curve, AUC_{inf}.

(Stip. Fact ¶ 91; JTX 6 at col. 12, ll. 12-22.)

52. Claim 6 depends from claims 1, 4 and 5, which add the following limitations: (a) "wherein the matrix is a polymer matrix" (claim 4); (b) "wherein the polymer matrix is comprised of a swellable, hydrophilic polymer" (claim 5); and (c) "wherein the gabapentin is released from the polymer matrix by diffusion" (claim 6). (Stip. Fact ¶¶ 90, 92-94; JTX 6 at col. 12, ll. 27-32.)

53. Claim 12 of the '332 Patent is directed to:

> A method of treating a condition responsive to a therapeutic dose of gabapentin, comprising: orally administering a dosage form, comprising a matrix comprising gabapentin, wherein upon ingestion of the dosage form gabapentin is released from the matrix into the upper gastrointestinal tract over about 5-12 hours at a rate sufficient to achieve a lower maximum plasma concentration than that provided by an immediate release dosage form comprising an equal amount of gabapentin, and bioavailability of gabapentin is at least 80% of that provided by the immediate release dosage form comprising an equal amount of gabapentin as measured by the area under the plasma concentration-time curve, AUC_{inf}.

(Stip. Fact ¶ 95; JTX 6 at col. 12, ll. 53-65.)

54. Claim 17 depends from claim 12, and adds the following limitations: the condition treated in the method is neuropathic pain (claim 17). (Stip. Fact ¶ 96; JTX 6 at col. 13, ll. 6-7.)

55. Claim 22 of the '332 Patent is directed to:

> A dosage form, comprising a matrix comprising gabapentin, wherein upon ingestion of the dosage form gabapentin is released from the matrix into the upper gastrointestinal tract over about 5-12 hours at a rate sufficient to achieve a longer time to the maximum plasma concentration than that provided by an immediate release dosage form comprising an equal amount of gabapentin, and bioavailability of gabapentin is at least 80% of that provided by the immediate release dosage form comprising an equal amount of gabapentin as measured by the area under the plasma concentration-time curve, AUC_{inf}.

(Stip. Fact ¶ 97; JTX 6 at col. 13, l. 21 – col. 14, l. 2.)

56. Claim 24 of the '332 Patent is directed to:

> A method of treating a condition responsive to a therapeutic dose of gabapentin, comprising orally administering a dosage form comprising a matrix comprising gabapentin, wherein gabapentin is released from the matrix into the upper gastrointestinal tract over about 5-12 hours at a rate sufficient to achieve a longer time to the maximum plasma concentration than that provided by an immediate release dosage form comprising an equal amount of gabapentin, and bioavailability of gabapentin is at least 80% of that provided by the immediate release dosage form comprising an equal amount of gabapentin as measured by the area under the plasma concentration-time curve, AUC_{inf}.

(Stip. Fact ¶ 98; JTX 6 at col. 14, ll. 16-29.)

6. U.S. Patent No. 8,333,992

57. The '992 Patent, entitled "Gastric Retained Gabapentin Dosage Form," issued on December 18, 2012, to Depomed from a patent application filed on July 27, 2012, as a continuation of the '927 Patent. (Stip. Fact ¶¶ 13, 99.) Depomed asserted claims 1, 5 and 22 of the '992 Patent. (Stip. Fact ¶ 100.)

58. Claim 1 of the '992 Patent is directed to:

> A dosage form, comprising a matrix comprising gabapentin, wherein upon ingestion of the dosage form by a human subject gabapentin is released from the matrix into the upper gastrointestinal tract over about 5-12 hours at a rate sufficient to achieve a lower maximum plasma concentration than that provided by an immediate release dosage form comprising an equal amount of gabapentin, and bioavailability of gabapentin is at least 80% of that provided by the immediate release dosage form comprising an equal amount of gabapentin as measured by the area under the plasma concentration-time curve, AUC_{inf}.

(Stip. Fact ¶ 102; JTX 7 at col. 12, ll. 40-51.)

59. Claim 5 depends from claim 4, which in turn depends from claim 1. Claims 4 and 5 add the following limitations: (a) "wherein the matrix is a polymer matrix" (claim 4); and (b) "wherein the polymer matrix is comprised of a swellable, hydrophilic polymer" (claim 5). (Stip. Fact ¶¶ 101, 103-104; JTX 7 at col. 12, ll. 56-59.)

60. Claim 22 of the '992 Patent is directed to:

> A method of treating a condition responsive to a therapeutic dose of gabapentin, comprising: orally administering to a human subject a dosage form comprising a matrix comprising gabapentin, wherein gabapentin is released from the matrix into the upper gastrointestinal tract over about 5-12 hours at a rate sufficient to achieve a longer time to the maximum plasma concentration than that provided by an immediate release dosage form comprising an equal amount of gabapentin, and bioavailability of gabapentin is at least 80% of that provided by the immediate release dosage form comprising an equal amount of gabapentin as measured by the area under the plasma concentration-time curve, AUC_{inf}.

(Stip. Fact ¶ 105; JTX 7 at col. 14, ll. 13-26.)

IV. WITNESSES PRESENTED AT TRIAL

A. Witnesses Supporting a Finding of Obviousness

1. Actavis' Case-In-Chief

61. Actavis put on its obviousness case-in-chief through the deposition testimony of a named inventor of the Gabapentin Patents, Sui Yuen Eddie Hou, Ph.D., and two expert witnesses, Douglas R. Flanagan, Jr., Ph.D. and Michael Mayersohn, Ph.D.

62. Dr. Sui Yuen Eddie Hou, a former Depomed employee and one of the named inventors of the Gabapentin Patents, testified via his deposition video regarding the development of the subject matter of the Gabapentin Patents. (5/14/2014 Tr. 547:24-548:1.)

63. Dr. Douglas R. Flanagan, a professor emeritus of pharmacy of the University of Iowa and the chief scientific officer for the University of Iowa's Pharmaceuticals Development Consortium, was accepted as an expert in pharmaceutical formulation, including the design and development of controlled release dosage forms. (5/14/2014 Tr. 549:20-22, 552:10-14.)

64. Dr. Michael Mayersohn, a professor of pharmaceutical sciences at the University of Arizona, College of Pharmacy, was accepted as an expert on drug absorption and pharmacokinetics. (5/15/2014 Tr. 688:14-15, 692:6-10.)

2. Depomed's Response

65. In its response case, Depomed called a total of seven expert witnesses, Hartmut Derendorf, Ph.D., Harold B. Hopfenberg, Ph.D., Howard Bockbrader, Ph.D., Barry Gidal, Pharm.D., Michelle Brown, M.D., Linda A. Felton, Ph.D. and Sean Nicholson, Ph.D. In addition, Depomed presented the testimony by deposition of one fact witness, Actavis employee Andrew Johnson, Ph.D. Depomed did not call or present deposition testimony from any of the inventors for the asserted patents.

66. Dr. Harold B. Hopfenberg, a professor of chemical and biomolecular engineering at North Carolina State University, was accepted as an expert in polymer science and controlled release dosage forms. (5/14/2014 Tr. 437:13-19.) Dr. Hopfenberg's testimony was limited to the '962 Patent.

67. Dr. Sean Nicholson, a professor in the Department of Policy Analysis and Management at Cornell University, was accepted as an expert in the field of economics in healthcare. (5/19/2014 Tr. 1061:20-25, 1064:5-7.) Dr. Nicholson testified regarding the alleged commercial success of the '962 Patent and the Gabapentin Patents.

68. Depomed's other expert witnesses were all called to testify regarding the Gabapentin Patents – the '927, '989, '756, '332 and '992 Patents.

69. Dr. Harmut Derendorf, a professor of pharmaceutics at the University of Florida, was accepted as an expert in pharmacokinetics. (5/13/2014 Tr. 332:20-22, 336:4-8.)

70. Dr. Howard Bockbrader, a former Warner-Lambert employee with a Ph.D. from Ohio State University, was accepted as an expert in the area of clinical pharmacokinetics, in particular the pharmacokinetics of gabapentin. (5/15/2014 Tr. 748:8-13.)

71. Dr. Barry Gidal, a professor of pharmacy at University of Wisconsin, Madison, was accepted as an expert on gabapentin pharmacokinetics and pharmacodynamics. (5/16/2014 Tr. 811:13-14, 815:14-816:2.)

72. Dr. Michelle Brown, staff anesthesiologist and pain management physician at Frye Regional Medical Center, North Carolina and Unifour Pain Treatment Center, North Carolina, was accepted as an expert in treating neuropathic pain. (5/16/2014 Tr. 866:16-19, 869:17-20.)

73. Dr. Linda A. Felton, a professor and chair of the Department of Pharmaceutical Sciences at the University of New Mexico, College of Pharmacy, was accepted as an expert in the area of controlled release dosage forms. (5/19/2014 Tr. 955:22-956:2, 959:1-4.)

74. Dr. Andrew Johnson, an Actavis employee, testified via his deposition video as to his role in the development of Actavis' ANDA Products. (5/20/2014 Tr. 1138:2-8.)

3. Actavis' Rebuttal

75. Actavis, in rebuttal, called two expert witnesses – Raymond Sinatra, M.D., Ph.D. and Ryan Sullivan, Ph.D.

76. Dr. Raymond Sinatra, director of anesthesiology and pain medicine at the VA Medical Center in West Haven, Connecticut, was accepted as an expert in pain medicine and the prescribing practices of physicians in pain management. (5/16/2014 Tr. 894:2-17, 895:21-24.)

77. Dr. Ryan Sullivan, a Ph.D. in economics from the University of California, San Diego, was accepted as an expert in the economics of intellectual property as it pertains to pharmaceutical products. (5/20/2014 Tr. 1165:3-5, 1165:25-1166:4.)

B. Witnesses Supporting a Finding of Noninfringement

1. Depomed's Case-In-Chief

78. Depomed, in its infringement case-in-chief against Actavis, called five expert witnesses – Eden Tesfu, Ph.D., Gary Annunziata, Ph.D., Robert O. Williams, Ph.D., Harmut Derendorf, Ph.D. and Harold B. Hopfenberg, Ph.D. – and three fact witnesses – Radi Hejazi, Ph.D., Meena Venugopal, Ph.D. and Depomed employee Mr. Jack Lee Anders. Depomed did not call or present deposition testimony from any of the inventors of any of the asserted patents.

79. Drs. Eden Tesfu, Gary Annunziata, Robert Williams and Hartmut Derendorf provided testimony regarding all of the asserted patents.

80. Dr. Eden Tesfu, a former employee of Evans Analytical Group Life Sciences ("EAG"), was accepted as an expert in the field of analytical chemistry and testified regarding an *in vitro* swelling study conducted on Actavis' ANDA Products ("the EAG swelling study"). (5/12/2014 Tr. 90:13-91:2, 92: 19-22.)

81. Dr. Gary Annunziata, a practicing gastroenterologist at the Eisenhower Medical Center, Palm Springs, California, was accepted as an expert in stomach physiology. (5/12/2014 Tr. 141:14-15, 148:12-14.)

82. Dr. Robert Williams, a professor at the University of Texas and a registered pharmacist in the State of Texas, was accepted as an expert in the field of formulation and pharmaceutical sciences. (5/13/2014 Tr. 261:9-262:1, 264:4-7.)

83. Dr. Harmut Derendorf, a professor of pharmaceutics at the University of Florida, was accepted as an expert in pharmacokinetics. (5/13/2014 Tr. 332:20-22, 336:4-8.)

84. Dr. Harold B. Hopfenberg, a professor of chemical and biomolecular engineering at North Carolina State University, was accepted as an expert in polymer science and controlled release dosage forms. (5/14/2014 Tr. 437:13-19.) Dr. Hopfenberg's testimony was limited to the '280 and '962 Patents.

85. Dr. Radi Hejazi, an Actavis employee, was involved in the development of Actavis' ANDA Products. (5/12/2014 Tr. 51:10-11, 19-22.)

86. Dr. Meena Venugopal, a former Actavis employee, was involved in the bioequivalence studies of Actavis' ANDA Products. (5/13/2014 Tr. 312:15-21.)

87. Mr. Jack Lee Anders, the Vice President of Finance at Depomed, testified as to commercial sales and licenses of the Gralise product and its predecessor patents. (5/13/2014 Tr. 378:4-22.)

2. Actavis' Response

88. In its response case, Actavis called one expert witness, David Friend, Ph.D.

89. Dr. David Friend, director of product development at the CONRAD Program and associate research professor of obstetrics and gynecology at Eastern Virginia Medical School, was accepted as an expert in the design and development of controlled release dosage forms, design and development of gastric retained dosage forms, behavior of dosage forms in the stomach during fed mode and the sizes and shapes of oral dosage forms. (5/14/2014 Tr. 498:9-12, 502:3-504:10.)

V. THE GABAPENTIN PATENTS ARE INVALID AS OBVIOUS.

A. Scope and Content of the Prior Art

1. Pharmacokinetic Properties for Controlled Release Formulations Were Well Known in the Prior Art.

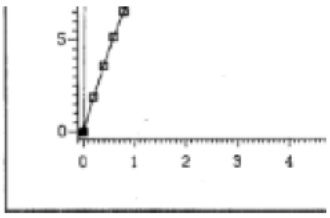
90. Dr. Mayersohn explained that pharmacokinetics is the measure of absorption, distribution, metabolism and exclusion/excretion of a drug. (5/15/2014 Tr. 732:19-22.) The pharmacokinetic parameters of a drug are specific to each drug. "One would not expect the numeric values to be similar, there is no reason. One does expect, and again, one of ordinary skill in the art would anticipate this, that the behavior, relative behavior, would be the same." (5/15/2014 Tr. 718:14-21.)

91. As Dr. Mayersohn explained, the pharmacokinetics of a drug are determined by administering the drug to a subject, drawing blood from the subject at predetermined times after administration and then determining the amount of drug found in the blood samples. Those data

are analyzed on a plot of the drug concentration (vertical axis) versus time (horizontal axis), such as the exemplary plot below:

Immediate Release
Formulation

Controlled Release
Formulation



(5/15/2014 Tr. 701:13-22; DTX 323 at GRALISE_JDG_00000574.) Drs. Mayersohn and Derendorf explained that, the maximum concentration of drug in the blood (i.e., the peak of the curve) is denoted C_{max}. The point of time at which the C_{max} is reached is denoted T_{max}. The total amount of drug absorbed is reflected by the area under the curve, denoted AUC or $AUC_{infinity}$. (5/15/2014 Tr. 693:25-695:3, 5/13/2014 Tr. 347:14-19.)

92. Dr. Mayersohn further explained that the taller curve is characteristic of an immediate release dosage form, whereas the shorter curve is characteristic of a controlled release version of the same drug. Put in terms of the pharmacokinetic parameters, Dr. Mayersohn explained that the controlled release dosage form (shorter curve) has a longer T_{max}, lower C_{max}

and at least comparable AUC as compared to the immediate release form of the same drug (taller curve). Drs. Flanagan and Mayersohn explained that these trends in the pharmacokinetic data comparing controlled and immediate release dosage forms are simply the natural result of a controlled release formulation that releases the drug more slowly and thus resulting in slower absorption of the drug. (Flanagan, Tr. 614:11-14.) As such, Dr. Flanagan testified that one of ordinary skill in the art would have routinely targeted these pharmacokinetic parameters (i.e., lower C_{max}, longer T_{max} and comparable AUC) in designing a controlled release version of an existing immediate release drug.

93. Dr. Flanagan and Dr. Mayersohn both testified that Shargel and Yu, APPLIED BIOPHARMACEUTICS AND PHARMACOKINETICS (1985) ("AB&P"), confirms that lowering C_{max} and extending T_{max} is the natural goal of every controlled release formulation, demonstrating that one of ordinary skill in the art would have known this and had these pharmacokinetic parameters as a goal in designing a controlled release dosage form. (5/14/2014 Tr. 574:4-575:1, 695:17-697:11; DTX 323 at GRALISE_JDG_00000573.) Dr. Mayersohn testified AB&P states that for a controlled release formulation "the time for peak concentration (T_{max}) is usually longer (Fig. 18-4) and the peak drug concentration (C_{max}) is reduced. If the drug is properly formulated, the area under the plasma drug concentration curve should be the same." (5/14/2014 Tr. 695:17-697:11; DTX 323 at GRALISE_JDG_00000573.)

2. Gastric Retained Dosage Forms for Highly Soluble Drugs Were Well Known in the Prior Art.

a) International Patent Publication No. WO 98/55107 (DTX 234)

94. International Patent Publication No. WO 98/55107 A1 ("Depomed's WO '107"), entitled *Gastric-Retentive Oral Drug Dosage Forms for Controlled Release of Highly Soluble Drugs*, was published on December 10, 1998 (5/14/2014 Tr. 556:4-12; DTX 234

at GRALISE_JDG_00000841), more than one year before the October 25, 2001 priority date of the Gabapentin Patents and the June 20, 2000 priority date of the '962 Patent. (5/19/2014 Tr. 955:1; DTX 234 at GRALISE_JDG_00000841.)

95. As Dr. Flanagan testified, Depomed's WO '107 later matured as a continuation-in-part to Depomed's '475 Patent, which will not expire until September 19, 2016. (5/15/2014 Tr. 685:11-14; see also DTX 234 at GRALISE_JDG_00000841 (showing the priority application of U.S. application No. 08/870,509); DTX 397 at GRALISE_JDG_00001235 (showing the '475 Patent is a continuation-in-part of application No. 08/870,509).)

96. Dr. Flanagan explained that the abstract for Depomed's WO '107 states that the purpose of the described dosage form is as follows:

> Drugs that are freely or highly soluble in water are formulated as unit dosage forms by incorporating them into polymeric matrices comprised of high molecular weight hydrophilic polymers that swell upon imbibition of water. The dosage form can be a single compressed tablet[]. . . . The oral formulation is designed for gastric retention and controlled delivery of an incorporated drug into the gastric cavity, and thus administered, the drug is released from the matrix into the gastric fluid by solution diffusion. The swollen polymeric matrix, having achieved sufficient size, remains in the gastric cavity for several hours if administered while the patient is in the fed mode, and remains intact long enough for substantially all of the drug to be released before substantial erosion of the matrix occurs . . . .

(5/14/2014 Tr. 556:22-557:8; DTX 234 at GRALISE_JDG_00000841.)

97. As Dr. Flanagan explained, Depomed's WO '107 states that the gastric retained dosage form for water soluble drugs is comprised of a polymeric matrix that remains substantially intact for a period of time that allows the majority of the drug to be released from the dosage form by diffusion:

> a formulation in which the drug is dispersed in a polymeric matrix that is water-swellable rather than merely hydrophilic, and that erodes at a rate that is substantially less than its swelling rate. It has further been found that the diffusion rate can be slowed by increasing the drug

> particle size, by the choice of polymer used in the matrix, or by the molecular weight of the polymer. The matrix is a relatively high molecular weight polymer that swells upon ingestion to achieve a size that is at least about twice its unswelled volume and that promotes gastric retention during the fed mode. . . .

(5/14/2014 Tr. 556:22-557:8; DTX 234 at GRALISE_JDG_00000844; see also id. at GRALISE_JDG_00000848 ("The release rate of a drug from the matrix is primarily dependent upon the rate of water imbibition and the rate at which the drug dissolves and diffuses from the swollen polymer.").) Dr. Flanagan further explained that Depomed's WO '107 has a diffusion rate can be slowed by increasing the drug particle size, by the choice of polymer used in the matrix, or by the molecular weight of the polymer. (5/15/2014 Tr. 615:6-13; DTX 234 at GRALISE_JDG_00000844.)

98. Dr. Flanagan explained that the matrix of Depomed's WO '107 dosage form is made of a water-swellable polymer "that swells in a dimensionally unrestricted manner upon imbibition of water." (5/14/2014 Tr. 555:9-16; DTX 234 at GRALISE_JDG_00000846.) The swelling of the polymeric matrix achieves two results:

> (i) it swells the matrix to a size large enough to cause it to be retained in the stomach during the fed mode, and (ii) it retards the rate of diffusion of a highly soluble drug long enough to provide multi-hour, controlled delivery of the drug into the stomach.

(5/15/2014 Tr. 683:14-21; DTX 234 at GRALISE_JDG_00000845.)

99. Depomed's WO '107 also explains that the "fed mode is initiated by the ingestion of food, and causes suspension of MMC [migrating motor complex] waves, thereby permitting the stomach to retain the particular matter long enough to be broken down and at least partially digested." (DTX 234 at GRALISE_JDG_00000850.) According to WO'107, administering the dosage form while in the fed mode is desirable:

> the dosage forms of the present invention find their greatest utility when administered to a subject who is in the digestive or "fed" mode".

> During this mode, particulate matter above a certain minimum particle size is retained in the subject's stomach.

(Id.) Dr. Flanagan testified the invention "provides enhanced absorption of soluble drugs that are absorbed mostly in the stomach or high in the gastrointestinal tract," by "providing a multi-hour flow of a drug" in that region, which is the most efficient absorption site for many agents. (5/14/2014 Tr. 557:1-8; DTX 234 at GRALISE_JDG_00000845.)

100. As Dr. Flanagan testified, Depomed's WO '107 states that its dosage form comprises "a solid polymeric matrix" in which the drug "is dispersed at a weight ratio of drug to polymer of about 80:20 or less." (5/14/2014 Tr. 557:1-8; DTX 234 at GRALISE_JDG_00000858.)

101. Depomed's WO '107 states that it is useful for drugs that are "at least 'freely soluble' in water, i.e., one part of the drug dissolves in less than about ten parts of water," and that "other drugs suitable for use and meeting the solubility parameters described above will be apparent to those skilled in the art." (Id. at GRALISE_JDG_00000846.) Exemplary drugs identified by Depomed's WO '107 are metformin hydrochloride, captopril, erythromycin lactobionate, ranitidine hydrochloride, sertraline hydrochloride and ticlopidine hydrochloride. (Id. at GRALISE_JDG_0000844.)

102. Depomed's WO '107 also explains that it provides a dosage form that will permit administration of highly soluble drugs in a manner "that will prolong their delivery time to extend substantially through the duration of the fed mode but not a substantial time beyond." (Id.)

103. Examples of suitable polymers for the invention of Depomed's WO '107 were listed by Dr. Flanagan as "methylcellulose, hydroxymethylcellulose, hydroxyethylcellulose, hydroxypropylcellulose, hydroxypropylmethylcellulose, and carboxymethylcellulose."

(5/15/2014 Tr. 636:16-19; DTX 234 at GRALISE_JDG_00000847.) Depomed's WO '107 further specified "[a] particularly preferred polyalkylene oxide is poly(ethylene oxide) ["PEO"]." (5/15/2014 Tr. 636:16-19; DTX 234 at GRALISE_JDG_00000847.) Depomed's WO '107 states that the molecular weights of preferred PEOs are "within the range of about 9 x 10^5 to about 8 x 10^6 . . . . Two presently preferred poly(ethylene oxide)s are POLYOX® NF, grade WSR Coagulant, molecular weight 5 million, and grade WSR 303, molecular weight 7 million." (DTX 234 at GRALISE_JDG_00000847.) Depomed's WO '107 explains that "[t]he hydrophilicity and water swellability characteristics of these polymers cause the drug-containing matrices to swell in size in the gastric cavity due to ingress of water in order to achieve a size that will be retained in the stomach when introduced during the fed mode." (Id. at GRALISE_JDG_0000848.)

104. Dr. Flanagan further testified that the amount of polymer in the dosage form of Depomed's WO '107 should:

> be sufficient however to retain at least about 40% of the drug within the matrix one hour after ingestion (or immersion in the gastric fluid). Preferably, the amount of polymer is such that at least 50% of the drug remains in the matrix one hour after ingestion. More preferably, at least 60%, and most preferably at least 80%, of the drug remains in the matrix one hour after ingestion.

(5/14/2014 Tr. 567:16-23; DTX 234 at GRALISE_JDG_0000848; see also, e.g., id. at GRALISE_JDG_0000858 (Claim 1), GRALISE_JDG_0000859 (claims 17, 18 and 19).) Depomed's WO '107 further explains that "[t]he amount of polymer relative to the drug can vary, depending on the drug release rate desired and on the polymer, its molecular weight and excipients that may be present in the formulation." (Id. at GRALISE_JDG_0000848.)

105. The Examples of Depomed's WO '107 illustrate how the choice of polymer can affect the release rate of drug from the dosage form. As Dr. Flanagan testified, Example 1 shows

how the time to release 90% of the drug could be varied from 3.5 hours to 7.5 hours by changing the molecular weight and concentration of the drug. (5/14/2014 Tr. 568:22-569:3; DTX 234 at GRALISE_JDG_00000851-52.) The other Examples illustrate the effect of substitutions of different polymers, addition of other excipients, changing the polymer to drug weight ratio, size of the dosage form and other factors on the release rate of the drug from the dosage form as determined by in-vitro dissolution assays. (Id. at GRALISE_JDG_00000852-57, GRALISE_JDG_00000861-68.) Dr. Flanagan explained that "[t]he water swellable polymers can be used individually or in combination" and "[c]ertain combinations will often provide a more controlled release of the drug than their components when used individually." (5/14/2014 Tr. 576:16-23; DTX 234 at GRALISE_JDG_00000848.) He further stated that the dissolution curves from the Examples are over five hours each. (5/14/2014 Tr. 567:14-18; DTX 234 at GRALISE_JDG_00000867 (Fig. 7).)

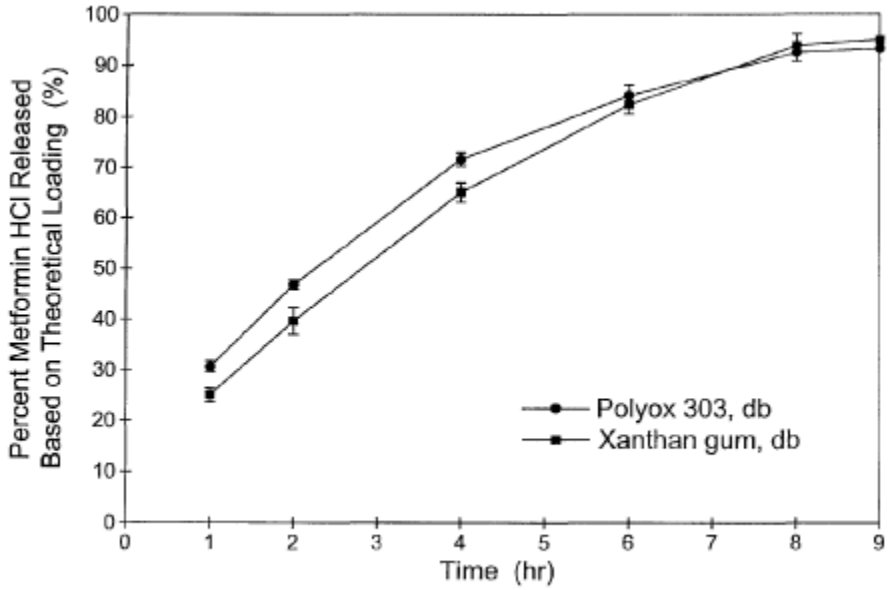


Fig. 7

(Id. at GRALISE_JDG_00000867.)

106. Dr. Flanagan testified that according to Depomed's WO '107, the dosage form should achieve effective results when administered "no more frequently than once every eight hours or more, preferably once every twelve hours or more, and even more preferably once every twenty-four hours or more." (5/14/2014 Tr. 567:24-568:2; DTX 234 at GRALISE_JDG_00000850.)

107. Dr. Flanagan explained the dosage forms of Depomed's WO '107 have different shapes, including non-circular shapes. (5/15/2014 Tr. 630:14-20, 633:22-634:1.) Depomed's WO '107 also discloses a non-circular tablet, an "elongated tablet with dimensions 18 to 22 mm in length, 6.5 to 7.8 mm in width, and 6.2 to 7.5 mm in height." (5/15/2014 Tr. 620:12-25; DTX 234 at GRAILSE_JDG_00000849.) In Example 5, Depomed's WO '107 also describes a tablet with dimensions of 6.48 mm, 7.20 mm and 19.21 mm. (DTX 234 at GRAILSE_JDG_00000854.) Depomed's WO '107 further states that the dimensions listed are "merely examples; the shapes and sizes can be varied considerably." (5/15/2014 Tr. 633:22-634:1; DTX 234 at GRALISE_JDG_00000849.)

108. Upon imbibition of water, Depomed's WO '107 dosage form swells, as Dr. Flanagan described, "to achieve a size that is at least about twice its unswelled volume." (5/15/2014 Tr. 631:15-18; DTX 234 at GRALISE_JDG_00000844.)

b) <u>International Patent Publication No. WO 99/47128 (DTX 236)</u>

109. International Patent Publication No. WO 99/47128 A1 ("WO '128"), entitled *Biphasic Controlled Release Delivery System for High Solubility Pharmaceuticals and Method*, was published on September 23, 1999, more than one year before the October 25, 2001 priority date of the Gabapentin Patents. (DTX 236 at GRALISE_JDG_00000055.)

110. WO '128 was not before the Examiner during the prosecution of the Gabapentin Patents. (See JTX 3; JTX 4; JTX 5; JTX 6; JTX 7 (WO '128 is not listed under "Foreign Patent Documents.")

111. As Dr. Mayersohn described, WO '128 is directed to:

> a new dosage form for highly water soluble medicaments, such as the antidiabetic metformin, which provides for extended release of the drug and prolonged gastric residence which enables efficient delivery of drugs normally absorbed in the upper gastrointestinal tract, and to a method for preparing such dosage form.

(5/15/2014 Tr. 698:8-14; DTX 236 at GRALISE_JDG_00000057.) This controlled release system "can be incorporated in a conventional systemic dosage form, such as a tablet or capsule." (DTX 236 at GRALISE_JDG_00000083.) WO '128 was further explained by Drs. Flanagan and Mayersohn as stating that its dosage forms are applicable to all drugs that have three properties: high water solubility, a limited window of absorption very high in the small intestine and absorbed by a saturable transport system. (5/15/2014 Tr. 626:22-627:1, 702:4-16, 714:15-17; DTX 236 at GRALISE_00000070.) Dr. Mayersohn stated that WO '128 defined "high water solubility" as "solubility in water at ambient temperature of at least about 50 mg/ml H_2O, preferably at least about 100 mg/ml H_2O or more, and more preferably greater than 150 mg/ml." (5/15/2014 Tr. 705:9-15; DTX 236 at GRALISE_JDG_00000072.) Dr. Flanagan further testified that WO '128 also states that "'limited window of absorption' . . . when characterizing a drug . . . for use in the formulation of the invention refers to an oral bioavailability of less than about 75%, usually less than about 60%, usually decreasing with increasing dose, and almost invariably having permeability/transit time limited absorption." (5/15/2014 Tr. 714:23-715:5; DTX 236 at GRALISE_JDG_00000072.)

112. WO '128 lists a wide variety of additional types of "high water soluble drugs" and "water-soluble drugs" that can be included in the described formulations. (DTX 236

at GRALISE_JDG_00000079-82.) The specification states that the oral bioavailability of metformin hydrochloride from immediate-release dosage forms was relatively low because of certain characteristics of the drug:

> Metformin hydrochloride has intrinsically poor permeability in the lower portion of the gastrointestinal tract leading to absorption almost exclusively in the upper part of the gastrointestinal tract. Its oral bioavailability is in the range of 40 to 60% decreasing with increasing dosage which suggests some kind of saturable absorption process, or permeability/transit time limited absorption. It also has a very high water solubility (>300 mg/ml at 25ºC). This can lead to difficulty in providing a slow release rate from a formulation and problems in controlling the initial burst of drug from such a formulation. These two difficulties are further compounded by the high unit dose, 500 mg per tablet, usually required for metformin hydrochloride (1997-PDR).

(Id. at GRALISE_JDG_00000057.)

113. Dr. Mayersohn further explained that WO '128 described "[d]rugs that have absorption limited to the upper gastrointestinal tract coupled with poor absorption in the distal small intestine, large intestine and colon are usually regarded as inappropriate candidates for formulation into oral controlled delivery systems. This limitation on absorption, for example, in the upper gastrointestinal tract, is referred to as the absorption window." (5/15/2014 Tr. 713:25-714:7; DTX236 at GRALISE_JDG_00000057-58.) Dr. Mayersohn further explained that WO '128 defines "limited window of absorption" as "oral bioavailability of less than about 75 percent, usually less than about 60 percent, usually decreasing, increasing dose and almost invariably having permeability/transit time limited absorption." (5/15/2014 Tr. 714:23-715:5; DTX236 at GRALISE_JDG_00000072.)

114. The formulation is described as having two benefits: "(a) [it] achieves extended gastric residence by virtue of size but will degrade in vivo so as not to have potential for causing gastric or intestinal obstruction, and (b) [it] controls drug release adequately where the initial burst of drug is under control." (Id.) The formulation "can be administered to various

mammalian species, such as dogs, cats, humans, etc., in need of such treatment." (Id. at GRALISE_JDG_00000082-83.)

115. Dr. Flanagan described the dosage form of WO '128 as:

> The finished dosage form is either a compressed tablet or a hard gelatin capsule, preferably a tablet. . . . The total amount of drug per dosage unit would be such as to offer a dosage form of convenient size for patients, but following ingestion would remain (or swell to, by hydration of the polymers used in the fabrication of the tablet) a size that does not easily pass through the pylorus (15 mm or greater) when taken with a meal. As the tablet swells up to approximately three times its dry size following hydration, drug loads of up to 750 mg are possible, dependent upon the actual characteristics of the individual drug.

(5/15/2014 Tr. 626:10-20; DTX 236 at GRALISE_JDG_00000086.)

116. WO '128 explains that "[t]ypical prior art techniques for creating a controlled release oral dosage form would involve either matrix systems or multiparticulate systems. Matrix systems may be formulated by homogenously mixing drug with hydrophilic polymers, such as hydroxypropylmethylcellulose, hydroxypropylcellulose, polyethylene oxide, carbomer, certain methacrylic acid derived polymers, sodium alginate, or mixtures of components selected from these . . . ." (DTX 236 at GRALISE_JDG_00000067.)

117. Dr. Flanagan described WO '128's dosage form as having "[a] swelling hydrogel polymer [that] has embedded within it drug particles that dissolve once the hydrogel matrix is hydrated. The swollen matrix is of a size to encourage gastric retention but only dissolved drug reaches the mucosa and this can be delivered in a sustained manner." (5/15/2014 Tr. 627:14-21; DTX 236 at GRALISE_JDG_00000066-67.) WO '128 states, as Dr. Flanagan explained, that "[i]n a controlled release dosage form, the formulator tries to reduce the rate of dissolution by, for example, embedding the drug in a polymeric matrix or surrounding it with a polymeric

barrier membrane through which drug must diffuse to be released for absorption." (5/15/2014 Tr. 627:14-21; DTX 236 at GRALISE_JDG_00000059.)

118. Dr. Flanagan further testified that "[o]n imbibing fluid[,] the system swells over a short period of time to a size that will encourage prolonged gastric retention, allowing sustained delivery of contained drug to absorption sites in the upper gastrointestinal tract." (5/15/2014 Tr. 626:15-20; DTX 236 at GRALISE_JDG_0000066.) Drs. Flanagan and Mayersohn testified that WO '128 states that it provides "a novel way . . . of formulating drug with high water solubility and a limited window of absorption such as [a drug] which has a window of absorption in the upper gastrointestinal tract, to provide a dosage form that inherently has prolonged gastric residence." (5/15/2014 Tr. 626:22-627:1, 704:20-705-1; DTX 236 at GRALISE_JDG_00000070.)

119. Dr. Mayersohn and Dr. Flanagan testified that a controlled release form of metformin was compared to its immediate release version (Glucophase) in Example 5 of WO '128. (5/15/2014 Tr. 617:10-618:15, 700:9-701:4.) The pharmacokinetic data reported in WO '128 were:

Formulation	Cmax (ng/ml)	AUC (inf) (ng.hr/ml)	Tmax*(hr)	%UR
Glucophase	1226(16)	10128(14)	3.5(1,5)	43.3(20)
Example 3	978(13)	10483(21)	5(4,8)	42.7(18)

*median (min., max.)

(DTX 236 at GRALISE_JDG_00000090.) Dr. Mayersohn and Dr. Flanagan testified that a comparison of these results shows that the controlled release version has a lower C_{max}, a longer

T_{max} and essentially the same bioavailability ($AUC_{infinity}$) as an immediate release dosage form containing the same dose of the same drug. (5/15/2014 Tr. 617:10-618:15, 700:9-701:4.)

3. Gabapentin, Its Properties and Its Therapeutic Uses Were Well Known in the Prior Art.

120. As named inventor Dr. Hou admitted, gabapentin is not a new drug and it was not developed by Depomed. (5/14/2014 Tr. 547:24-548:1.) Rather, Gabapentin was conceived of and synthesized in the early 1970s by Goedecke, A.G., in Germany, which was part of Warner-Lambert at the time. (Stip. Fact ¶ 117; 5/16/2014 Tr. 857:3-9.) Warner-Lambert gained FDA approval of and commercialized Neurontin®, an immediate release formulation of gabapentin, in December 1993 – nearly a decade before the priority dates of the Patents-In-Suit. (Stip. Fact ¶ 119; 5/15/2014 Tr. 686:1-5.)

a) Therapeutic Uses of Gabapentin

121. Depomed was also not the first to develop gabapentin to treat postherpetic neuralgia, as testified to by Dr. Hou. (5/14/2014 Tr. 548:3-5.)

122. When Neurontin was first approved in the United States, it was indicated "as adjunctive therapy in the treatment of partial seizures with and without secondary generalization in patients over 12 years of age with epilepsy. Neurontin is also indicated as adjunctive therapy in the treatment of partial seizures in pediatric patients age 3 - 12 years." (DTX 291 at GRALISE_JDG_00000158.)

123. There was a significant amount of research in the 1990's regarding other uses of gabapentin beyond the treatment of epilepsy. (5/15/2014 Tr. 672:22-24.) For example, Rowbotham, which was published before the October 25, 2001 priority date of the Gabapentin Patents, concluded that Neurontin was effective for the treatment of neuropathic pain, such as

postherpetic neuralgia, painful diabetic neuropathy and other types of neuropathic pain. (See, e.g., DTX 313; Tr. 5/14/2014 Tr. 559:4-560:5; 5/16/2014 Tr. 857:3-8.)

b) Therapeutically Effective Doses of Gabapentin

124. As Dr. Flanagan testified, gabapentin was known in the prior art to be an effective treatment of neuropathic pain, with daily doses ranging from 300 mg/day to 3,600 mg/day. (5/14/2014 Tr. 559:4-560:5; 5/15/2014 Tr. 619:11-14, 622:17-623:3; DTX 313 at GRALISE_JDG_00000452 (Study participants "began with an initial dose of 300 mg/d" which was then "increased over the next four weeks (titration period) in a step-up manner (900, 1800, 2400, and 3600 mg/d divided three times a day), to a maximum total dose of 3600 mg/d."), GRALISE_JDG_00000451 ("Conclusions—Gabapentin is effective in the treatment of pain and sleep interference associated with [postherpetic neuralgia].").)

125. With respect to the treatment of epilepsy, Dr. Flanagan recited the Neurontin Label as stating:

> effective dose of Neurontin® is 900 to 1800 mg/day and given in divided doses (three times a day) using 300 or 400 mg capsules, or 600 or 800 mg tablets. The starting dose is 300 mg three times a day. If necessary, the dose may be increased using 300 or 400 mg capsules, or 600 or 800 mg tablets three times a day up to 1800 mg/day. Dosages up to 2400 mg/day have been well tolerated in long-term clinical studies. Doses of 3600 mg/day have also been administered to a small number of patients for a relatively short duration, and have been well tolerated."

(5/15/2014 Tr. 620:15-24; DTX 291 at GRALISE_JDG_00000169.)

c) Pharmacokinetics of Gabapentin

126. Dr. Gidal admitted that from the treatment of patients suffering from epilepsy or postherpetic neuralgia with immediate release gabapentin, gabapentin's pharmacokinetic properties became well known in the prior art. (516/2014 Tr. 858:7-11; see also 5/14/2014 Tr. 547:24-548:5.) Dr. Flanagan testified that one of skill in the art would have been fully aware

of the C_{max}, T_{max} and $AUC_{infinity}$ ranges of immediate-release gabapentin that were effective to treat patients suffering with neuropathic pain because this information was known in the prior art and could be gathered from the literature. (5/15/2014 Tr. 686:1-9.)

127. Depomed's experts, Dr. Gidal and Dr. Derendorf, agreed with Dr. Flanagan that the pharmacokinetic data for gabapentin in the treatment of postherpetic neuralgia was well known in the prior art. (5/16/2014 Tr. 858:7-11; 5/19/2014 Tr. 1048:16-1049:1.)

128. The Neurontin Label discloses the oral bioavailability of gabapentin, stating:

> [g]abapentin bioavailability is not dose proportional; i.e., as dose is increased, bioavailability decreases. A 400 mg dose, for example, is about 25% less bioavailable than a 100 mg dose. Over the recommended dose range of 300 to 600 mg T.I.D., however, the differences in bioavailability are not large, and bioavailability is about 60 percent. Food has only a slight effect on the rate and extent of absorption of gabapentin (14% increase in AUC and C_{max}).

(DTX 291 at GRALISE_JDG_00000153.)

129. The '927 Patent specification acknowledges that it was known in the art that higher doses of gabapentin after administration of immediate release gabapentin tablets and capsules had poorer bioavailability than lower doses. (JTX 3 at col. 1, ll. 13-22.)

130. As Dr. Flanagan explained that it was known by one of ordinary skill in the art that gabapentin's half-life was "relatively short," which was "potentially problematic from a compliance perspective," suggesting that most individuals would require three daily doses, but that "[a]vailability of a slow-release formulation might permit twice daily dosing, also." (5/14/2014 Tr. 558:5-559:3; DTX 267 at GRALISE_JDG_00000130.)

d) <u>Absorption of Gabapentin</u>

131. By October 25, 2001, it was well known that gabapentin was absorbed by a saturable carrier-mediated process high in the gastrointestinal tract. (5/14/2014 Tr. 558:5-559:3, 560:6-561:9; 5/15/2014 Tr. 711:18-22.) The '927 Patent specification acknowledges that various

prior art described the absorption of gabapentin from the gastrointestinal tract. (JTX 3 at col. 1, ll. 22-37.)

132. As Drs. Flanagan and Mayersohn explained, saturable absorption means that the transporters can only bring in a certain amount of drug at any given time. (5/14/2014 Tr. 563:19-24; 5/15/2014 Tr. 710:11-17.) If more than that amount of drug reaches the transporter, then the additional amount of drug will not be absorbed. (5/14/2014 Tr. 563:19-24; 5/15/2014 Tr. 710:11-17.)

133. Dr. Flanagan testified that gabapentin was known in the prior art to exhibit saturable absorption, and that this absorption occurred primarily in the upper gastrointestinal tract. (5/14/2014 Tr. 560:6-561:9, 564:22-565:1; PTX 500 at GRALISE_JDG_00000601, 603; DTX 267 at GRALISE_JDG_00000127.) Dr. Mayersohn similarly confirmed that gabapentin's absorption occurs by a saturable process that is characteristic of transporters. (5/15/2014 Tr. 713:12-16.) Dr. Mayersohn testified that it was known in the prior art that absolute bioavailability of gabapentin is dose dependent because of facilitated transport by the L-amino acid transporter. (5/15/2014 Tr. 711:18-22, 712:17-19; DTX 266 at GRALISE_JDG_00000469; DTX 267 at GRALISE_JDG_00000127.) Dr. Mayersohn stated that "the literature seems pretty clear and consistent that this drug's absorbed high up in the small intestine. There seems to be a so-called window of absorption, a limited range over which the drug can be absorbed." (5/15/2014 Tr. 708:24-709:9, 713:3-6, 713:12-16; DTX 298 at GRALISE_JDG_00001073.) He further explained that it was known in the prior art both that the absorption of gabapentin in the colon was very low and that gabapentin had a narrow window of absorption in the duodenum. (5/15/2014 Tr. 706:25-707:3, 707:23-708:6; DTX 419 at GRALISE_JDG_00001028; PTX 500 at GRALISE_JDG_00000602.)

134. The prior art confirms the opinions of Drs. Flanagan and Mayersohn. For example, Stevenson states that "increasing the oral dose of gabapentin has been shown to result in a decreased fraction of absorbed dose suggesting saturable absorption." (5/15/2014 Tr. 713:3-6; PTX 500 at GRALISE_JDG_00000603.) Furthermore, Stevenson studied the absorption of gabapentin at various locations in the gastrointestinal tract of dogs. (PTX 500 at GRALISE_JDG_00000601, 605.) As Dr. Flanagan testified, Stevenson observed that a "[c]omparison of the blood-level data from oral and jejunal administration of gabapentin indicates that there is substantial absorption from the duodenum and upper jejunum. (5/14/2014 Tr. 560:6-561:9; PTX 500 at GRALISE_JDG_00000601.) Most important, [however,] gabapentin plasma levels from colonic administration are substantially lower than those obtained from oral and upper intestinal administration (Fig. 1 and Table 1)." (PTX 500 at GRALISE_JDG_00000601.) Stevenson concluded that "[c]olonic gabapentin absorption is poor compared with upper intestinal absorption, consistent with membrane transport rate limits to the absorption of this hydrophilic [drug]." (See id. at GRALISE_JDG_00000601.) Stevenson further observed that "[i]ncreasing the oral dose of gabapentin has been shown to result in a decreased fraction of absorbed dose, suggesting saturable absorption." (Id. at GRALISE_JDG_00000603.)

135. The prior art also explains that gabapentin was absorbed by saturable transporters high in the gastrointestinal tract. For example, Dr. Mayersohn testified that McLean states that gabapentin "is transported across the gut wall by the L system amino acid transporter," and that the "[a]bsolute bioavailability of gabapentin is dose-dependent, probably as a result of the saturable absorption by the L system amino acid transporter." (5/15/2014 Tr. 711:18-22; DTX 267 at GRALISE_JDG_00000127.) Dr. Mayersohn also testified that Vollmer states that

"[t]he site of [gabapentin] absorption was not the stomach but the duodenum." (5/15/2014 Tr. 706:25-707:3; DTX 419 at GRALISE_JDG_00001028.) Dr. Annunziata explained that the duodenum is the portion of the small intestine that is situated just after the stomach. (5/12/2014 Tr. 152:11-153:1.)

136. Even Depomed's own experts, Dr. Derendorf and Dr. Bockbrader, admitted that it was known in the prior art that gabapentin was absorbed by transporters, that they exhibited saturable absorption, and were primarily absorbed in the upper gastrointestinal tract, such as the duodenum. (See 5/13/2014 Tr. 351:11-16; 361:4-7, 362:10-12; 5/19/2014 Tr. 961:19-20, 1055:20-1056:7; 5/15/2014 Tr. 748:22-749:3, 759:21-25; PTX 271 at DEPOACT0966661, DEPOACT0966663.)

B. The Level of Ordinary Skill in the Art

137. A person of ordinary skill in the art is defined as "a person with a Ph.D. in chemistry, chemical engineering, pharmaceutical sciences or a related discipline. Alternatively, the person could have a master's degree in one of those fields with at least two years of practical experience and alternatively, the person could have a bachelor's degree in one of those fields with even more practical experience." (5/14/2014 Tr. 553:17-24.) This person, having the education and experience described, would be knowledgeable about different dosage forms, including gastric retained forms, the pharmacokinetics of those dosage forms, and the relevant indications for the different drugs and dosage forms, amongst other issues. Actavis' experts, namely Drs. Flanagan and Mayersohn, both meet this definition. (5/14/2014 Tr. 553:25-554:2; 5/15/2014 Tr. 688:13-692:5.)

138. Depomed's definition of a person of ordinary skill in the art is not materially different from this definition (5/19/2014 Tr. 932:17-25) and both parties' experts agree that their

respective opinions would not change if the other party's definition were used. (5/14/2014 Tr. 554:6-555:1; 5/19/2014 Tr. 933:11-13.)

C. The Asserted Claims of the Gabapentin Patents Would Have Been Obvious.

139. Actavis asserts that the asserted claims of the Gabapentin Patents would have been obvious to one of ordinary skill over Depomed's WO '107 (DTX 234) in view of an article by Michael Rowbotham (DTX 313), along with the knowledge of a person of ordinary skill in the art. (D.I. 327 at 21-23.)

140. Actavis also asserts that the asserted claims of the '332 and '992 Patents would have been obvious to one of ordinary skill over WO '128 (DTX 236) and the Rowbotham article (DTX 313), along with the knowledge of a person of ordinary skill in the art. (D.I. 327 at 21-23.)

1. The Asserted Claims of the '927 Patent Would Have Been Obvious in View of Depomed's WO '107 and Rowbotham.

a) Depomed's WO '107 and Rowbotham Disclose All of the Limitations of Claims 17 and 33 of the '927 Patent.

141. All asserted claims of the '927 Patent depend from and thus incorporate all of the limitations of one of two independent claims – claim 17 or claim 33 – neither of which is asserted in the litigation. Depomed's WO '107 discloses all of the limitations of claims 17 and 33 of the '927 Patent except for those relating to treating patients with particular doses of gabapentin.

142. A named inventor of the '927 Patent, Dr. Hou, acknowledged during his deposition that Depomed did not invent gabapentin or its use to treat conditions such as neuropathic pain. (5/14/2014 Tr. 547:24-548:1, 548:3-5.) Thus, the therapeutic uses for

gabapentin recited in the claims is nothing more than the recitation of known uses for gabapentin that were elucidated by others, such as Warner-Lambert.

143. With respect to the limitations "[a] method of treating neuropathic pain in a mammal comprising administering a therapeutically effective amount of a daily dosage of about 100 mg to about 4800 mg of gabapentin or a pharmaceutically acceptable salt thereof," Dr. Flanagan testified those aspects are described in Rowbotham. (5/14/2014 Tr. 559:4-560:5.) Rowbotham explains that daily doses of up to 3600 mg gabapentin per day were effective to treat pain and sleep interference associated with post-herpetic neuralgia, a type of neuropathic pain. (5/14/2014 Tr. 559:4-560:5; DTX 313 at GRALISE_JDG_00000451-452.)

144. Dr. Flanagan explained that Depomed's WO '107 discloses an orally administered, gastric retained, controlled release formulation for use with a highly soluble drug when "administered to a subject who is in the digestive or 'fed' mode." (5/14/2014 Tr. 556:4-12; DTX 234 at GRALISE_JDG_0000084, GRALISE_JDG_00000850, GRALISE_JDG_00000841 (the "swollen polymeric matrix, having achieved sufficient size, remains in the gastric cavity for several hours if administered while the patient is in the fed mode, and remains intact long enough for substantially all of the drug to be released before substantial erosion of the matrix occurs").)

145. Dr. Flanagan further explained that Depomed's WO '107 discloses that the "drug is dispersed in a polymeric matrix, and that matrix is water swellable." (5/14/2014 Tr. 556:22-557:8; DTX 234 at GRALISE_JDG_00000845.) Dr. Flanagan testified that Depomed's WO '107 goes on to state that the "water swellable polymer forming the matrix . . . is any polymer . . . that swells in a dimensionally unrestricted manner upon imbibition of water, and that provides for sustained release of an incorporated drug." (5/14/2014 Tr. 556:22-557:8; DTX 234 at GRALISE_JDG_00000846, GRALISE_JDG_00000848 ("The hydrophilicity and

water swellability of these polymers cause the drug-containing matrices to swell in size in the gastric cavity . . . in order to achieve a size that will be retained in the stomach when introduced during the fed mode.").) Depomed's WO '107 further discloses that the "matrix is a relatively high molecular weight polymer that swells upon ingestion to achieve a size that is at least about twice its unswelled volume and that promotes gastric retention during the fed mode." (5/14/2014 Tr. 556:22-557:8; DTX 234 at GRALISE_JDG_00000844, GRALISE_JDG_00000841 ("matrices comprised of high molecular weight hydrophilic polymers that swell upon imbibition of water.").) The matrix polymers disclosed in Depomed's WO '107 are "water swellable rather than merely hydrophilic" (DTX 234 at GRALISE_JDG_00000844) and include such well-known hydrophilic polymers as "cellulose polymers and their derivatives, polysaccharides and their derivatives, polyalkylene oxides, and crosslinked polyacrylic acids and their derivatives." (DTX 234 at GRALISE_JDG_00000847.) Examples of well-known cellulose polymers include hydroxypropylmethylcellulose, hydroxymethylcellulose, and hydroxypropylcellulose, among others. (Id.) Examples of well-known polyalkylene oxides include polyethylene oxide. (Id.)

146. As defined by Dr. Flanagan, Depomed's WO '107 discloses that "the drug is [then] released from the matrix into the gastric fluid by solution diffusion." (5/14/2014 Tr. 556:22-557:8; DTX 234 at GRALISE_JDG_00000841, GRALISE_JDG_00000858 (claim 1) ("releases said drug into gastric fluid by the dissolution and diffusion of said drug out of said matrix by said gastric fluid").)

147. Specifically, the Figures of Depomed's WO '107 are plots of dissolution data for the formulations in the Examples. These dissolution curves show that drug is released for at least five hours from the dosage forms. For example, in Figure 7, less than all of the drug was released after 5 hours:

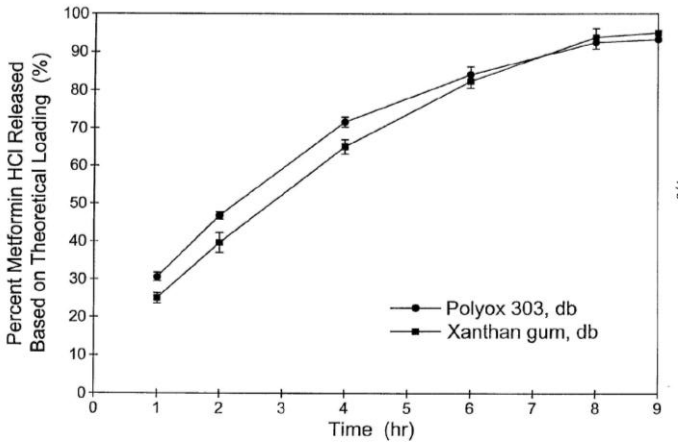


Fig. 7

(DTX 234 at GRALISE_JDG_00000867.) The further increase in drug release after five hours indicates that drug continued to be released for at least five hours.

148. As Dr. Flanagan explained, Depomed's WO '107 discloses that the:

> amount of polymer [in the dosage form] will be sufficient . . . to retain at least about 40% of the drug within the matrix one hour after ingestion (or immersion in the gastric fluid). Preferably, the amount of polymer is such that at least 50% of the drug remains in the matrix one hour after ingestion. More preferably, at least 60%, and most preferably at least 80%, of the drug remains in the matrix one hour after ingestion.

(5/14/2014 Tr. 556:22-557:8; DTX 234 at GRALISE_JDG_00000848, GRALISE_JDG_00000858 (claim 1) ("upon immersion in gastric fluid retains at least about 40% of said drug one hour after such immersion").)

149. Furthermore, with respect to the frequency of administering the dosage form, Dr. Flanagan testified that Depomed's WO '107 discloses once daily dosing. He explained that Depomed's WO '107 states that "[i]n most cases, the dosage form will be such that effective results will be achieved with administration no more frequently than once every eight hours or more, preferably once every twelve hours or more, and even more preferably once every twenty-four hours or more." (5/14/2014 Tr. 567:24-568:2; DTX 234 at GRALISE_JDG_00000850.)

b) One of Ordinary Skill in the Art Would Be Motivated to Combine Depomed's WO '107 and Rowbotham.

150. Although Depomed's WO '107 does not explicitly mention gabapentin, one of ordinary skill in the art would have been motivated to formulate gabapentin in Depomed's WO '107 gastric retained dosage form.

151. All of the experts agree that one of ordinary skill in the art in 2001 would have been motivated to make a controlled release gabapentin formulation to alleviate the burden on patients to take multiple doses per day, improve patient compliance, and reduce the incidence of side effects. (5/15/2014 Tr. 751:11-18; 5/19/2014 Tr. 963:21-964:1; 5/14/2014 Tr. 558:5-559:3; 5/16/2014 Tr. 873:12-22; DTX 267 at GRALISE_JDG_00000130.)

152. By October 2001, it was also known in the art that gabapentin is highly water soluble and absorbed high in the gastrointestinal tract through a saturable carrier-mediated system. (5/15/2014 Tr. 686:1-5, 702:4-7; 5/16/2014 Tr. 845:24; 5/19/2014 Tr. 963:2-6; DTX 267 at GRALISE_JDG_00000126-28.) Based on these properties of gabapentin, a person of ordinary skill in the art would understand that a conventional controlled release dosage form that releases drug along the entire length of the gastrointestinal tract would be inappropriate for gabapentin. (5/15/2014 Tr. 637:2-6, 702:4-16, 713:22-714:17, 769:24-770:3.) Instead, as Dr. Felton explained, one of ordinary skill would have known that a gastric retentive system would have been the only viable approach to make a controlled release form of gabapentin because it would hold the gabapentin in a place above its window of absorption for an extended period of time. (5/19/2014 Tr. 964:15-965:16.)

153. Named inventor, Dr. Hou, confirmed that it was in fact these known absorption characteristics that made gabapentin such a good candidate for a gastric retained, controlled

release dosage form. (5/14/2014 Tr. 548:11-14.) Dr. Hou explained that non-gastric retained dosage forms were not even considered for gabapentin. (Id. at 548:15-17.)

154. Dr. Flanagan described WO '107 as:

> The invention . . . provides enhanced absorption of soluble drugs that are absorbed mostly in the stomach or high in the gastrointestinal tract, such as metformin hydrochloride or ciprofloxacin. The invention is also useful in providing a multi-hour flow of a drug past the upper part of the small intestine (the most efficient absorption site for many agents).

(5/14/2014 Tr. 556:22-557:8; DTX 234 at GRALISE_JDG_00000845.) Because gabapentin is similarly absorbed primarily high in the gastrointestinal tract and is water soluble, Dr. Flanagan stated that one of ordinary skill in the art would consider Depomed's WO '107 dosage form a suitable one for gabapentin. (5/14/2014 Tr. 557:9-25.)

155. As testified to by Dr. Flanagan, one of ordinary skill in the art would also have had a motivation to replace metformin in the gastric retained formulations disclosed in Depomed's WO '107 with gabapentin because both drugs were known to exhibit saturable absorption high in the gastrointestinal tract. (5/14/2014 Tr. 564:22-565:1.) Dr. Flanagan testified that, if a drug is only absorbed in a certain region of the gastrointestinal tract, i.e. has a specific window of absorption, then one has to develop a formulation that will release it in the region where it will be absorbed and that drugs with similar windows of absorption would be expected to be absorbed similarly if they were placed in the same formulation. (Id. at 564:15-21.) And Depomed's experts Drs. Derendorf and Felton both explained that a controlled release gastric retained dosage form would improve issues relating to saturation, by slowing down the release of drug and thus avoiding overwhelming the transporters with a large amount of drug. (5/13/2014 Tr. 364:13-15; 5/19/2014 Tr. 1010:1-14.)

156. Depomed argues that there was no motivation to put gabapentin in Depomed's WO '107 dosage form because: (1) gabapentin is not explicitly mentioned in Depomed's WO '107; (2) metformin is a different drug from gabapentin; (3) gabapentin degrades to lactam in stomach acid; (4) gabapentin absorption is variable between individuals; (5) there was no established relationship between gabapentin's pharmacokinetics and its pharmacodynamics (i.e., clinical efficacy); and (6) the dosage form requires administration with food, which can affect gabapentin absorption.

157. Although gabapentin is not explicitly mentioned, Depomed's WO '107 dosage form is described as being useful for drugs that are soluble and have a window of absorption high in the gastrointestinal tract and is not limited to any particular drug. (DTX 234 at GRALISE_JDG_0000845.) That Depomed's WO '107 lists a number of exemplary drugs having different physical and chemical properties that can be used in the dosage form, such as metformin, erythromycin, vancomycin, ranitidine and captopril, further supports this conclusion. (Id. at GRALISE_JDG_00000846.) There is no reason therefore that one of ordinary skill in the art would understand Depomed's WO '107 to be limited to metformin or the drugs specifically identified in Depomed's WO '107.

158. Furthermore, that metformin is chemically different from gabapentin (5/16/2014 Tr. 845:17-18; 5/19/2014 Tr. 1043:12-23) is irrelevant in view of Depomed's WO '107 disclosure. Depomed's WO '107 states that the high water solubility and absorption primarily occurring high in the gastrointestinal tract are the significant characteristics of drugs suitable for incorporation in Depomed's WO '107 dosage form. (DTX 234 at GRALISE_JDG_00000845.) Gabapentin has these characteristics, just like metformin.

159. Although Drs. Felton and Gidal suggest that one of ordinary skill in the art would not be motivated to formulate gabapentin in Depomed's WO '107 dosage form because of its propensity to slowly degrade in certain environments such as those found in the stomach (5/16/2014 Tr. 856:1-6, 856:9-14; 5/19/2014 Tr. 1009:15-20), both acknowledge that the prior art provides a solution for the lactam issues. Dr. Gidal admitted that gabapentin's lactam degradation was discovered and previously solved by Warner-Lambert, who received a patent on that solution. (5/16/2014 Tr. 858:12-18.) Dr. Felton also admitted that she did not consider Depomed's own disclosures in International Publication No. WO 93/18755 ("WO '755"), which states that hydrophilic polymer matrices can protect drugs from being degraded in stomach acid by being trapped in the dry core of the tablet until it is dissolved and released by penetrating gastric fluid. (5/19/2014 Tr. 1009:15-20; DTX 230 at GRALISE_JDG_00000900.) Thus, the possibility of lactam formulation would not have reduced or removed the motivation of one of ordinary skill in the art to put gabapentin in Depomed's WO '107 dosage form, given that this issue had been previously solved in the prior art.

160. Depomed's experts, Drs. Gidal and Bockbrader, also stated that there is significant variability between individuals in their ability to absorb gabapentin. But Depomed's experts came forward with no evidence that this variability had any impact on gabapentin's clinical efficacy. To the contrary, it would be surprising if there was such an effect, given that the immediate release gabapentin product was a blockbuster drug for Warner-Lambert, with sales exceeding a billion dollars per year at its peak. (5/16/2014 Tr. 865:10-12.) Dr. Felton never considered that variability in absorption never stopped sales of Neurontin. (Id. at 1010:20-24.) Thus, inter-person variability in gabapentin absorption would not impact the motivation one

of ordinary skill in the art would have to formulate gabapentin in Depomed's WO '107 dosage form.

161. Depomed's experts also argue that there was no known relationship between gabapentin's pharmacokinetics and its pharmacodynamics (or clinical efficacy), ignoring that an immediate release gabapentin product had been commercially available for more than seven years before Depomed applied for the Gabapentin Patents. (See *supra*, ¶ 143.) Through clinicians' and researchers' experiences with gabapentin, the pharmacokinetics of gabapentin, as well as effective doses of gabapentin, had become well known in the art. (See *supra*, ¶¶ 126-130.) Dr. Derendorf explained that this experience with immediate release gabapentin would provide a target that formulators would seek to obtain using a controlled release formulation. (5/19/2014 Tr. 1049:13-16.) Moreover, even today, the pharmacokinetic – pharmacodynamic relationship for gabapentin has not been determined. (5/20/2014 Tr. 1214:16-19.) Yet, this has not stopped Depomed, Pfizer, and generic pharmaceutical manufacturers from bringing various gabapentin products to the U.S. market. Thus, the absence of a known pharmacokinetic – pharmacodynamic relationship is not probative.

162. Finally, notwithstanding that the literature states that food has no clinically significant effect on gabapentin, Drs. Bockbrader, Gidal, and Felton all suggested that a food effect would have cast doubt on motivation to create a gastric retained formulation of gabapentin. (5/15/2014 Tr. 775:20-776:6; 5/16/2014 Tr. 817:19-20, 831:8-13, 833:23-834:2, 840:7-8; 5/16/2014 Tr. 962:24-963:1, 1010:25-1011:3.) Dr. Bockbrader later admitted that the food effect was not clinically significant. (5/15/2014 Tr. 776:2-11.) Dr. Gidal also admitted to not knowing whether the alleged food effect was of any clinical significance, and that the food effect did not stop Neurontin from becoming a blockbuster drug for Pfizer. (5/16/2014

Tr. 865:5-9.) Dr. Felton admitted that any food effect just was not a major concern. (5/19/2014 Tr. 1013:16-19.) In fact, the Neurontin label says gabapentin can be taken with or without food. (DTX 291 at GRALISE_JDG_00000169.) Thus, to the extent food impacted gabapentin's bioavailability, it would not have affected the motivation that one of ordinary skill in the art would have had to put gabapentin in Depomed's WO '107 dosage form.

163. Depomed also argues that WO '812 teaches away from a matrix dosage form being gastric retained without an attached membrane system. (5/15/2014 Tr. 653:2-25.) WO '812 does not criticize, however, swellable gastric-retained dosage forms, much less the dosage form described in Depomed's WO '107. Instead, WO '812 merely provides an alternative way of causing a dosage form to be gastric retained. (DTX 229 at GRALISE_JDG_00002877.) In addition, WO '812 is not focused on highly soluble drugs. Instead the dosage form is for drugs with a narrow window of absorption, including those that "are poorly soluble at intestinal medium pH," drugs intended for local treatment in the gastrointestinal tract or drugs that degrade in the colon. (Id. at GRALISE_JDG_00002880-82.)

c) One of Ordinary Skill in the Art Would Have Had a Reasonable Expectation of Success in Combining Depomed's WO '107 and Rowbotham.

164. Dr. Flanagan testified that one of ordinary skill "would have taken gabapentin and put it into one or more of Depomed's WO '107 formulations and they would have had a reasonable expectation that they would have had an efficiently absorbed gastric retained formulation." (5/14/2014 Tr. 577:5-8.) Depomed's WO '107 states that any number of water soluble drugs (with significantly different chemical and physiological properties) with limited absorption high in the gastrointestinal tract can be formulated into Depomed's WO '107 dosage form. (Id. at 557:9-25.) Given the similarity between gabapentin's solubility and absorption high in the gastrointestinal tract (see DTX 234 at GRALISE_JDG_00000126-28) to the drugs

described in Depomed's WO '107, one of ordinary skill in the art would have had a reasonable expectation of success in formulating Depomed's WO '107 dosage form with gabapentin. (5/14/2014 Tr. 565:2-5.)

165. That the absorption of both gabapentin and metformin was known to be saturable would further provide a person of ordinary skill in the art with a reasonable expectation of success in substituting gabapentin for metformin in the formulations disclosed by Depomed's WO '107, as testified by Dr. Flanagan. (5/14/2014 Tr. 564:22-565:1.) Dr. Flanagan testified that if a drug is only absorbed in a certain region of the gastrointestinal tract, i.e. has a specific window of absorption, then one has to develop a formulation that will release it in the region where it will be absorbed. He also explained that drugs with similar windows of absorption would be expected to be absorbed similarly if they were placed in the same formulation. (Id. at 564:15-21.)

166. Furthermore, Dr. Flanagan explained that placing a drug in a controlled release formulation releases it in such a way as to avoid saturating the transporter. (Id. at 564:5-12.) Drs. Derendorf and Felton echoed this in testifying that a controlled release gastric retained dosage form would ameliorate issues associated with absorption of a drug through saturable transporters. (5/13/2014 Tr. 364:13-15; 5/19/2014 Tr. 1010:1-14.) Thus, one of ordinary skill in the art would expect that the bioavailability of gabapentin would be improved by slowing the release of gabapentin in a controlled release dosage form such as Depomed's WO '107 dosage form.

167. Dr. Flanagan further testified that a person of ordinary skill would have expected a therapeutic effect for the controlled release formulation as compared to the known immediate release formulation. (5/14/2014 Tr. 577:19-578:1.) Effective daily doses (e.g., 300 mg to

4,800 mg) of gabapentin to treat epilepsy or neuropathic pain were well known to those of skill in the art in October 2001. (See generally DTX 267 at GRALISE_JDG_00000126-28; DTX 313 at GRALISE_JDG_00000451, GRALISE_JDG_00000453-56.) Furthermore, Dr. Flanagan testified both 300 mg and 600 mg once-daily dose strengths would have been a natural starting points for one skilled in the art for creating a once-a-day formulation. (5/15/2014 Tr. 619:21-620:1, 622:1-14.) This is because a 300 mg of gabapentin per day dose was the known starting point to treat postherpetic neuralgia, and Dr. Flanagan testified that 600 mg of gabapentin per day would be a reasonable second dose strength for the purposes of titration – a process by which the dose of a drug administered to a patient is increased over time. (Id. at 621:3-14, 622:17-623:3; DTX 313 at GRALISE_JDG_00000452.) Dr. Flanagan testified that other strengths, such as 1800 mg of gabapentin in a single tablet, would not be used because the size of the tablet would be too large for a person to swallow. (5/15/2014 Tr. 623:4-13.)

168. In addition to the arguments addressed above with respect to the motivation to combine prior art references, Depomed raised the following additional issues to argue that one of ordinary skill in the art would not have a reasonable expectation of success: (1) gabapentin may not actually be gastric retained in vivo and thus may not be made available in its narrow window of absorption; and (2) gabapentin's release rate may not avoid saturation of absorption of transporters.

169. As explained by Dr. Flanagan, Depomed's WO '107 explains, however, that the dosage form "is designed for gastric retention." (5/14/2014 Tr. 557:1-2; DTX 234 at GRALISE_JDG_00000841). This is accomplished by the dosage form "swell[ing] to a size large enough to cause it to be retained in the stomach during the fed mode." (Id. at GRALISE_JDG_00000845, GRALISE_JDG_00000848 ("The hydrophilicity and water

swellability of these polymers cause the drug-containing matrices to swell in size in the gastric cavity due to ingress of water in order to achieve a size that will be retained in the stomach when introduced in the fed mode.").) Depomed's WO '107 also explains that the swelling of the polymeric matrix "retards the rate of diffusion of a highly soluble drug long enough to provide multi-hour, controlled delivery of the drug into the stomach." (Id. at GRALISE_JDG_00000845.) This permits "a multi-hour flow of a drug past the upper part of the small intestine" where gabapentin is most efficiently absorbed. (Id.)

170. Furthermore, Depomed's speculation that Depomed's WO '107 may not actually be gastric retained and deliver its payload to be absorbed in the upper gastrointestinal tract is inconsistent with its description of Depomed's WO '107 in the Gabapentin and '962 Patents and the disclosures in Depomed's WO '107 itself. For example, in the specification of the Gabapentin Patents, Depomed states that Depomed's WO '107 dosage form is "particularly tailored to be gastric-retained dosages," and "suitable for use in delivering gabapentin in the method of the invention." (JTX 3 at col. 5, ll. 52-60.) In the '962 Patent specification, Depomed cites to Depomed's WO '107 as a "[d]isclosure[] of oral dosage forms that swell to sizes that will prolong the residence time in the stomach." (Id. at col. 2, ll. 52-67.)

171. Furthermore, Dr. Flanagan testified that Depomed's WO '107 discloses "gastric retentive oral dosage forms for controlled release of highly soluble drugs." (5/14/2014 Tr. 556:4-12; DTX 234.) Depomed's WO '107 was filed in the PTO by Depomed on June 5, 1998. (DTX 234 at GRALISE_JDG_00000841.) 37 C.F.R. § 1.68 requires each inventor to submit an oath or declaration attesting that "all statements made of the declarant's own knowledge are true and that all statements made on information and belief are believed to be true." It is reasonable to infer from the requirement in 37 C.F.R. § 1.68 that the named inventors

of Depomed's WO '107 did indeed make true statements in their disclosures in Depomed's WO '107. It is reasonable to infer, therefore, that Depomed's WO '107 does disclose gastric retentive oral dosage forms for controlled release of highly soluble drugs, despite Depomed's speculation otherwise. It is unreasonable for Depomed to question the accuracy of statements contained in its very own WO '107.

172. It is also reasonable to infer from the requirement in 37 C.F.R. § 1.68 that the named inventors of Gabapentin Patents and '962 Patent also made true statements in their disclosures in their characterization of Depomed's WO '107. It is unreasonable, therefore, for Depomed to question the accuracy of statements contained in their very own Gabapentin Patents and '962 Patent.

173. In addition, the Gabapentin Patents' shared specification provides that "[t]here are several drug delivery systems that are suitable for use in delivering gabapentin in the method of the invention as they are particularly tailored to be gastric-retained dosages, such as . . . the swellable, hydrophilic polymer system described in Shell, et al., U.S. Pat. No. 5,972,389 and Shell, et al., WO 9855107; all of which are incorporated herein by reference." (JTX 3 at col. 5, ll. 52-62.) The specification later elaborates that in one

> embodiment of the invention, the gastric retained dosage form of gabapentin is an extended release oral drug dosage form for releasing gabapentin into the stomach, duodenum and small intestine of a patient, and comprises: a single or a plurality of solid particles consisting of gabapentin or a pharmaceutically acceptable salt thereof dispersed within a polymer that (i) swells unrestrained dimensionally by imbibing water from gastric fluid to increase the size of the particles to promote gastric retention in the stomach of the patient in which the fed mode has been induced; (ii) gradually the gabapentin diffuses or the polymer erodes over a time period of hours, where the diffusion or erosion commences upon contact with the gastric fluid; and (iii) releases gabapentin to the stomach, duodenum and small intestine of the patient, as a result of the diffusion or polymeric erosion at a rate corresponding to the time period. Exemplary polymers include polyethylene oxides,

> alkyl substituted cellulose materials and combinations thereof, for example, high molecular weight polyethylene oxides and high molecular weight or viscosity hydroxypropylmethylcellulose materials. Further details regarding an example of this type of dosage form can be found in Shell, et al., U.S. Pat. No. 5,972,389 and Shell, et al., WO 9855107.

(Id. at col. 6, l. 50 - col. 7, l. 5.)

174. Furthermore, Depomed's concerns with avoiding saturation of the transporters are addressed by the prior art. Drs. Derendorf and Felton explained that slowing the release of drug from a gastric retained dosage form would reduce any saturation of the saturable transporters. (5/13/2014 Tr. 364:13-15; 5/19/2014 Tr. 1010:1-14.) Depomed's WO '107 further explains that the "release rate of a drug from the matrix is primarily dependent upon the rate of water imbibition and the rate at which the drug dissolves and diffuses from the polymer, which in turn is related to the solubility and dissolution rate of the drug, the drug particle size and the drug concentration in the matrix." (DTX 234 at GRALISE_JDG_00000848.) The Examples of Depomed's WO '107 illustrate how modulating particle size, and the drug to polymer ratio, among other parameters, can affect the drug release rate. [redacted]

Thus, one of skill in the art would understand that putting gabapentin in Depomed's WO '107 dosage form would cause gabapentin to be released at a slower rate, which would mitigate or overcome any issues associated with saturation of the transporters.

175. Drs. Hopfenberg and Felton suggested that Hwang (DTX 222) would have cast doubt on an expectation of success. (5/19/2014 Tr. 947:16-948:17, 968:15-973:3.) Hwang, as admitted by both those experts, did not even consider Depomed's WO '107 prior art publication

because Hwang was published before Depomed's WO '107. (5/19/2014 Tr. 954:17-955:1, 1006:6-9.) Thus, Hwang could not cast doubt on an expectation of success after the later publication of Depomed's WO '107.

176. Dr. Flanagan summarized, "gabapentin was a known drug with known properties and known therapeutic uses." (5/14/2014 Tr. 553:6-7.) It was known in the prior art to use dosage forms with swellable polymers to obtain controlled release and gastric retention of soluble drugs with narrow absorption windows, and "a person of skill in the art would have had a reasonable expectation of success putting gabapentin in a prior art dosage form." (Id. at 553:8-12.)

177. For these reasons, claims 17 and 33 of the '927 Patent would have been obvious to one of ordinary skill in the art. (5/14/2014 Tr. 555:9-20, 569:21-23.)

d) Asserted Dependent Claims 18, 25, 26, 34, 61 and 62 of the '927 Patent Would Have Been Obvious in View of Depomed's WO '107 and Rowbotham.

178. The six asserted claims of the '927 Patent, claims 18, 25, 26, 34, 61 and 62 depend from either independent claim 17 or claim 33. Thus, the discussion above with respect to claims 17 and 33 applies to claims 18, 25, 26, 34, 61 and 62 as well.

179. Claim 18 of the '927 Patent incorporates the limitations of claim 17, and claim 34 of the '927 Patent incorporates the limitations of claim 33. Both claims 18 and 34 further require that "the dosage form is administered once-daily." (JTX 3 at col. 12, ll. 52-53, col. 13, ll. 40-41.) This additional limitation of claims 18 and 34 is described in Depomed's WO '107. Specifically, as explained by Dr. Flanagan, Depomed's WO '107 discloses that effective results will be achieved by administering its dosage form once every 24 hours. (5/14/2014 Tr. 565:6-9; DTX 234 at GRALISE_JDG_00000850 ("In most cases, the dosage form will be such that effective results will be achieved with administration no more frequently than . . . preferably

once every twelve hours or more, and even more preferably once every twenty-four hours or more.").) Accordingly, claims 18 and 34 would have been obvious over the same prior art discussed above with respect to claims 17 and 33. (5/14/2014 Tr. 566:18-20.)

180. Claim 25 of the '927 Patent incorporates the limitations of claim 17 and further requires that "the gastric retained dosage form release gabapentin to the stomach, duodenum and small intestine." (JTX 3 at col. 13, ll. 1-3.) This additional requirement of claim 25 is disclosed in Depomed's WO '107. Dr. Flanagan explained that Depomed's WO '107 states that the claimed dosage form is "useful in providing a multi-hour flow of a drug past the upper part of the small intestine (the most efficient absorption site for many agents)." (5/14/2014 Tr. 565:2-5; DTX 234 at GRALISE_JDG_00000845 ("The invention also provides enhanced absorption of soluble drugs that are absorbed mostly in the stomach or high in the gastrointestinal tract."), GRALISE_JDG_00000857 (Example 8) ("By providing for all or at least a portion of the total administered amount to be delivered by controlled delivery in the gastric retentive system of this invention, that portion so delivered is directed to the proximal portion of the small intestine.").) Thus, as Dr. Flanagan explained, claim 25 would have been obvious for these reasons and the reasons discussed above with respect to claims 17 and 33. (5/14/2014 Tr. 568:10-13.)

181. Claim 26 of the '927 Patent incorporates the limitations of claim 17 and further requires that "the dosage form provides administration of at least 85 wt % of the gabapentin to be delivered over a period of about 5-12 hours." (JTX 3 at col. 13, ll. 4-6.) This additional limitation of claim 26 is found in Depomed's WO '107. Specifically, Depomed's WO '107 discloses that a drug is released from the matrix in about eight hours. (DTX 234 at GRALISE_JDG_00000848 ("In all cases, however, the drug will be substantially all released from the matrix within about eight hours after ingestion."), GRALISE_JDG_00000851

(Example 1) ("Three different dose levels were prepared – systems designed to release 90% of their drug contents at approximately 3 hours, 6 hours and 8 hours, respectively," which was confirmed by in vitro dissolution testing), GRALISE_JDG_00000861 (results in Fig. 1).) At most, obtaining the release profile set out in claim 26 of the '927 Patent would require no more than routine optimization by one of ordinary skill following the teachings of the prior art. (5/15/2014 Tr. 633:3-7.) And the Examples of Depomed's WO '107 provide guidance to those skilled in the art like Dr. Flanagan as to how parameters such as the size of the dosage form, the ratio of drug to polymer in the formulation, and the presence of other excipients can alter the rate at which a drug is released from Depomed's WO '107 dosage form. Thus, claim 26 would have been obvious for these reasons and the reasons discussed above with respect to claims 17 and 33. (5/14/2014 Tr. 568:10-13.)

182. Claim 61 of the '927 Patent incorporates the limitations of claim 17, and claim 62 of the '927 Patent incorporates the limitations of claim 33. Both claims 61 and 62 further require that "the mammal is a human." (JTX 3 at col. 14, ll. 50-53.) This additional limitation of claims 61 and 62 is present in Depomed's WO '107. Specifically, Depomed's WO '107 discloses that its claimed dosage form is given to patients or subjects in the fed mode. (DTX 234 at GRALISE_JDG_00000841, GRALISE_JDG_00000850.) Furthermore, Rowbotham discloses the administration of gabapentin to human patients for the treatment of neuropathic pain. (DTX 313 at GRALISE_JDG_00000451.) In any event, humans are an obvious target for pharmaceutical products. Thus, as Dr. Flanagan explained, claims 61 and 62 would have been obvious for these reasons and the reasons discussed above with respect to claims 17 and 33. (5/14/2014 Tr. 570:8-10.)

2. The Asserted Claim of the '989 Patent Would Have Been Obvious in View of Depomed's WO '107 and Rowbotham.

183. The only asserted claim from the '989 Patent, claim 10, depends from independent claim 1, which is not being asserted. Independent claim 1 of the '989 Patent shares many common requirements with claim 17 of the '927 Patent. The limitations of claim 1 of the '989 Patent are substantially identical to the limitations found in claim 17 of the '927 Patent. (5/14/2014 Tr. 570:18-24.) Accordingly, claim 1 of the '989 Patent would have been obvious to one of ordinary skill in the art for the same reasons stated above with respect to claim 17 of the '927 Patent. (5/14/2014 Tr. 570:25-571:3.)

184. Claim 10 of the '989 Patent depends from claim 1 and further requires that "gabapentin has a bioavailability greater than or equal to 80% of an equal dose of gabapentin in an immediate release dosage form." (JTX 4.)

185. Although Depomed's WO '107 does not expressly disclose this limitation, Dr. Flanagan testified that those of skill in the art routinely designed controlled release dosage forms to have a bioavailability of at least 80% of an equal dose of the drug in an immediate release dosage form. (5/14/2014 Tr. 574:4-575:1.) Dr. Mayersohn testified AB&P states that for a controlled release formulation "the area under the plasma drug concentration curve should be the same" for an immediate release formulation compared to a controlled release formulation. (5/14/2014 Tr. 695:17-697:11; DTX 323 at GRALISE_JDG_00000574.) Dr. Flanagan testified that this is the target of all controlled release dosage forms to ensure that the controlled release dosage form had similar efficacy to multiple dosings of the immediate release dosage forms. (5/14/2014 Tr. 577:11-15.)

186. Given what was known in the prior art about the pharmacokinetic properties of immediate release gabapentin, one skilled in the art would have had an expectation that a

controlled release form of gabapentin would have at least 80% or more of the bioavailability of an immediate release formulation containing the same amount of gabapentin. (Id. at 575:7-576:7; DTX 5 at GRALISE_JDG_00000146.) This is because slowing the rate of release of the drug would avoid saturation of the transporters (5/13/2014 Tr. 364:13-15; 5/19/2014 Tr. 1010:1-14), meaning that less of the gabapentin would get past the site of absorption in the upper gastrointestinal tract without being absorbed.

187. In any event, Dr. Flanagan testified that bioavailability greater than or equal to 80% of an equal dose of gabapentin in an immediate release dosage form could be achieved by one of ordinary skill through routine optimization. (5/14/2014 Tr. 577:9-15.) Dr. Flanagan testified one of ordinary skill would have a reasonable expectation that the therapeutic effect of this dosage form would be equivalent to an immediate release dosage form when the two dosage forms had roughly equivalent bioavailability over the dosing interval. (Id. at 577:19-578:1.)

188. For these reasons, and the reasons discussed above with respect to the '927 Patent, claim 10 of the '989 Patent would have been obvious to one of ordinary skill in the art. (Id. at 573:10-13.)

3. The Asserted Claims of the '756 Patent Would Have Been Obvious in View of Depomed's WO '107 and Rowbotham.

189. Depomed asserted claims 1, 2, 5, 6, 7 and 11 of the '756 Patent. (Stip. Fact ¶ 79.)

a) Independent Claims 1 and 6 Would Have Been Obvious in View of Depomed's WO '107 and Rowbotham.

190. Claim 6 is related to claim 1 as being a method of treating a condition responsive to a therapeutic dose of gabapentin by orally administering an oral dosage form having the requirements of claim 1 either once-daily or twice-daily. (JTX 5.) The other differences to the claims are not substantial and will be addressed together.

191. The only claim element from claims 1 and 6 of the '756 Patent that has not been previously discussed in the context of the '927 and '989 Patents, above, is the requirement that "gabapentin is released at a rate sufficient to achieve a lower maximum plasma concentration (C_{max}) compared to an equal dose of gabapentin provided by an immediate release dosage form." (JTX 3; JTX 4; JTX 5.)

192. Although Depomed's WO '107 does not explicitly state that its formulation achieves a reduced C_{max}, Dr. Flanagan explained that those of skill in the art routinely designed controlled release dosage forms to have a lower C_{max} than an immediate release dosage form. (5/15/2014 Tr. 614:19-615:1.) Dr. Flanagan testified that one skilled in the art would have understood the claim element "the maximum plasma concentration or C_{max}" as the natural result of a controlled release formulation that's releasing its drug slowly and being absorbed slowly. (Id. at 614:8-18.) Even Depomed's Dr. Derendorf testified that a controlled release drug would release the drug slower (5/13/2014 Tr. 362:16-18), resulting in a lower C_{max} (id. at 364:23-365:3) and a longer T_{max}. (Id. at 365:16-21.) Thus, one of ordinary skill would have expected the claimed outcome from using Depomed's WO '107 formulations in comparison to an immediate release formulation.

193. Dr. Flanagan and Dr. Mayersohn both testified that Shargel and Yu, APPLIED BIOPHARMACEUTICS AND PHARMACOKINETICS (1985) ("AB&P"), confirms that lowering C_{max} and extending T_{max} is the natural goal of every controlled release formulation, demonstrating that one of ordinary skill in the art would have known this and had these pharmacokinetic parameters as a goal in designing a controlled release dosage form. (5/14/2014 Tr. 574:4-575:1, 695:17-697:11; DTX 323 at GRALISE_JDG_00000573.) Dr. Mayersohn testified that AB&P states that for a controlled release formulation "the time for peak concentration (T_{max}) is usually longer

(Fig. 18-4) and the peak drug concentration (C_{max}) is reduced. If the drug is properly formulated, the area under the plasma drug concentration curve should be the same." (5/14/2014 Tr. 695:17-697:11; DTX 323 at GRALISE_JDG_00000573.) Even Depomed's expert, Dr. Derendorf, testified that a controlled release drug would have a lower C_{max} than an immediate release drug, a concept that was known in the prior art. (5/13/2014 Tr. 364:23-365:3, 1049:24-1050:8.)

194. Dr. Flanagan also testified that formulating a controlled release dosage form to have a lower C_{max} compared to an immediate release dosage form would have been within the skill of a person of ordinary skill in the art. (5/15/2014 Tr. 682:16-19.) [redacted]

Furthermore, Depomed's WO '107 provides guidance in its examples as to how to modulate characteristics of the dosage form, such as the size of the dosage form, the relative amounts of drug and polymer and the other excipients in the dosage form, to obtain the desired rate of drug release. (DTX 234 at GRALISE_JDG_00000844, GRALISE_JDG_00000848.) Thus, obtaining a lower C_{max} would be, at most, a matter of routine optimization for one of ordinary skill in the art. (5/15/2014 Tr. 618:21-619:2.)

195. For these reasons, and the reasons discussed above with respect to the '927 Patent, independent claims 1 and 6 of the '756 Patent would have been obvious to one of ordinary skill in the art. (5/15/2014 Tr. 615:14-17.)

b) Dependent Claims 2, 5, 7 and 11 of the '756 Patent Would Have Been Obvious In View of Depomed's WO '107 and Rowbotham.

196. The four additional asserted claims of the '756 Patent, claims 2, 5, 7 and 11 depend from either independent claims 1 or 6. (JTX 5.) Thus, the discussion above with respect to claims 1 and 6 equally applies to claims 2, 5, 7 and 11.

197. Claims 2 and 7 depend from independent claims 1 and 6 respectively. (Id.) Both claims 2 and 7 further require that "the time to reach maximum plasma concentration is longer relative to the time to reach maximum plasma concentration from an immediate release dosage form comprising the dose of gabapentin." (Id. at col. 13, ll. 4-7, col. 14, ll. 1-4.)

198. This additional limitation of claims 2 and 7 is nothing more than, as Dr. Flanagan stated, "a natural result of a controlled release formulation releasing the drug more slowly than an immediate-release formulation." (5/15/2014 Tr. 616:19-617:5.) AB&P states that, for a controlled release formulation, "the time for peak concentration (T_{max}) is usually longer" than for an immediate release formulation of the same drug. (DTX 323 at GRALISE_JDG_00000573.) Dr. Flanagan testified that Depomed's WO '107 also provides guidance as to achieving longer T_{max}. (5/15/2014 Tr. 618:19-619:2; DTX 234 at GRALISE_JDG_00000844.) Thus, for these reasons and the reasons above with respect to claims 1 and 6, Dr. Flanagan explained that claims 2 and 7 would have been obvious over the prior art. (5/15/2014 Tr. 615:18-616:1.)

199. Claim 5 of the '756 Patent incorporates the limitations of claim 1 and further requires that the dosage form comprise "a dose of gabapentin of between about 300-600 mg." (JTX 5 at col. 13, ll. 12-13.) Effective doses (e.g., 300 to 4,800 mg) of gabapentin to treat epilepsy or neuropathic pain were well known to those of skill in the art in October 2001. (See generally 5/15/2014 Tr. 755:17-21; 5/16/2014 Tr. 830:22-25; DTX 267 at GRALISE_JDG_00000126-28; DTX 313 at GRALISE_JDG_00000451, GRALISE_JDG_00000453-56.) Furthermore, both 300 mg and 600 mg once-daily dose strengths would have been natural starting points for one skilled in the art for creating a once-a-day formulation, as testified to by Dr. Flanagan. (5/15/2014 Tr. 619:21-620:1, 622:1-14.) This is because a 300 mg/day dose was the known starting point to treat postherpetic neuralgia, and

Dr. Flanagan testified that 600 mg/day would be a reasonable second dose strength for the purposes of titration – a process by which the dose of a drug administered to a patient is increased over time. (Id. at 621:3-14, 622:17-623:3; DTX 313.) Thus, for these reasons and the reasons above with respect to claims 1 and 6, claim 5 would have been obvious over the prior art. (5/15/2014 Tr. 619:6-14.)

200. Claim 11 of the '756 Patent incorporates the limitations of claim 6 and further requires that "the condition is neuropathic pain." (JTX 5 at col. 14, ll. 10-11.) One of ordinary skill in the art in October 2001 knew that gabapentin was used to treat neuropathic pain. (5/16/2014 Tr. 857:3-9; DTX 313 at GRALISE_JDG_00000451 ("gabapentin is effective in the treatment of pain and sleep interference associated with PHN [postherpetic neuralgia]," a type of neuropathic pain), GRALISE_JDG_00000453-56.) The use of gabapentin is merely the use of a known drug for one of its known purposes – i.e., as a treatment of neuropathic pain. Thus, for these reasons and the reasons above with respect to claim 6, claim 11 would have been obvious over the prior art. (5/15/2014 Tr. 623:17-23.)

201. For these reasons, and the reasons discussed above with respect to the '927 and '989 Patents, claims 2, 5, 7 and 11 of the '756 Patent would have been obvious to one of ordinary skill in the art. (Id. at 615:18-616:1, 619:6-14, 623:17-23.)

4. The Asserted Claims of the '332 and '992 Patents Would Have Been Obvious to One of Ordinary Skill in the Art.

202. Depomed asserted claims 1, 6, 17, 22 and 24 of the '332 Patent. (Stip. Fact ¶ 89.) Of these claims, claims 1, 22 and 24 are independent claims. Claim 6 depends from and incorporates all the limitations of claim 1. Claim 17 depends from and incorporates all the limitations of unasserted claim 12.

203. The following chart summarizes the similarities between the asserted claims of the '332 Patent.

Claim 1 '332 Patent	Claim 12 '332 Patent	Claim 22 '332 Patent	Claim 24 '332 Patent
	A method of treating a condition responsive to a therapeutic dose of gabapentin, comprising: orally administering		***A method of treating a condition responsive to a therapeutic dose of gabapentin, comprising orally administering***
A dosage form, comprising a matrix comprising gabapentin,	a dosage form, comprising a matrix comprising gabapentin,	A dosage form, comprising: a matrix comprising ***300 mg or 600 mg*** of gabapentin,	a dosage form comprising a matrix comprising gabapentin,
wherein upon ingestion of the dosage form	wherein upon ingestion of the dosage form	wherein upon ingestion of ***one 600 mg*** dosage form ***or two 300 mg dosage forms***	wherein
gabapentin is released from the matrix into the upper gastrointestinal tract over about 5-12 hours at a rate sufficient to achieve a ***lower*** maximum plasma concentration than that provided by an immediate release dosage form comprising an equal amount of gabapentin, and	gabapentin is released from the matrix into the upper gastrointestinal tract over about 5-12 hours at a rate sufficient to achieve a ***lower*** maximum plasma concentration than that provided by an immediate release dosage form comprising an equal amount of gabapentin, and	gabapentin is released from the matrix into the upper gastrointestinal tract over about 5-12 hours at a rate sufficient to achieve a ***longer time to the*** maximum plasma concentration than that provided by an immediate release dosage form comprising an equal amount of gabapentin, and	gabapentin is released from the matrix into the upper gastrointestinal tract over about 5-12 hours at a rate sufficient to achieve a ***longer time to the*** maximum plasma concentration than that provided by an immediate release dosage form comprising an equal amount of gabapentin, and

Claim 1 '332 Patent	Claim 12 '332 Patent	Claim 22 '332 Patent	Claim 24 '332 Patent
bioavailability of gabapentin is at least 80% of that provided by the immediate release dosage form comprising an equal amount of gabapentin as measured by the area under the plasma concentration-time curve, AUC_{inf}.	bioavailability of gabapentin is at least 80% of that provided by the immediate release dosage form comprising an equal amount of gabapentin as measured by the area under the plasma concentration-time curve, AUC_{inf}.	bioavailability of gabapentin is at least 80% of that provided by the immediate release dosage form comprising an equal amount of gabapentin as measured by the area under the plasma concentration-time curve, AUC_{inf}.	bioavailability of gabapentin is at least 80% of that provided by the immediate release dosage form comprising an equal amount of gabapentin as measured by the area under the plasma concentration-time curve, AUC_{inf}.

204. Depomed also asserts claims 1, 5 and 22 of the '992 Patent. (Stip. Fact ¶ 100.) Claims 1 and 22 are independent claims. Claim 5 depends indirectly from claim 1.

205. Claims 1 and 22 of the '992 Patent differ from claims 1 and 24 of the '332 Patent, respectively, only with respect to the requirement that the '992 Patent claims require administering the dosage form to a human subject. (JTX 6; JTX 7.) Because these claims are essentially identical, the claims of the '332 and '992 Patents will be discussed together.

a) Independent Claims 1, 12, 22 and 24 of the '332 Patent and Claims 1 and 22 of the '992 Patent Would Have Been Obvious in View of Depomed's WO '107 and Rowbotham.

206. As discussed above with respect to the '927, '989 and '756 Patents, the combination of WO'107 and Rowbotham discloses most of the requirements of claims 1, 12, 22 and 24 of the '332 Patent and claims 1 and 22 of the '992 Patent. For example, Depomed's WO '107 discloses a dosage form that has a matrix containing an active ingredient, as Dr. Flanagan testified. (5/14/2014 Tr. 556:22-557:8; DTX 234 at GRALISE_JDG_00000844-45.) Dr. Flanagan explained that because the dosage form is gastric retained, it releases its drug payload to the upper gastrointestinal tract. (5/14/2014 Tr. 557:1-8; DTX 234 at GRALISE_JDG_00000845.) And, as the figures in Depomed's WO '107 demonstrate, the dosage form releases drug over a period of about five to eight hours. (5/14/2014 Tr. 567:14-18;

DTX 234 at GRALISE_JDG_00000867 (Fig. 7).) Moreover, Rowbotham explains that gabapentin can be used to treat various conditions in humans including postherpetic neuralgia, and discloses effective daily doses of 300 mg, 600 mg or even more of gabapentin, as Dr. Flanagan testified. (5/14/2014 Tr. 559:4-560:5; 5/15/2014 Tr. 622:17-623:3; DTX 313 at GRALISE_JDG_00000452.)

207. Each of the asserted claims of the '332 and '992 Patents each include two of the following three pharmacokinetic requirements:

i. at a rate sufficient to achieve ***a lower maximum plasma concentration*** than that provided by an immediate release dosage form comprising an equal amount of gabapentin (claims 1 and 12 of the '332 Patent and claim 1 of the '992 Patent);

ii. at a rate sufficient to achieve ***a longer time to the maximum plasma concentration*** than that provided by an immediate release dosage form comprising an equal amount of gabapentin (claims 22 and 24 of the '332 Patent and claim 22 of the '992 Patent); and

iii. ***bioavailability of gabapentin is at least 80%*** of that provided by the immediate release dosage form comprising an equal amount of gabapentin ***as measured by the area under the plasma concentration-time curve, AUC_{inf}*** (required by all asserted claims of the '332 and '992 Patents).

208. Although Depomed's WO '107 does not expressly disclose the specific pharmacokinetic parameters recited in the asserted claims of the '332 and '992 Patents for gabapentin, as already discussed above for the '989 and '756 Patents, one of skill in the art would have been motivated to achieve drug release without loss in bioavailability, a longer T_{max} and a lower C_{max} when compared to an immediate release dosage form of gabapentin and would have had a reasonable expectation of success in achieving these characteristics using no more than routine optimization techniques in the art. (See, *supra*, ¶¶ 192-194.) In fact, as Dr. Flanagan testified, the claimed pharmacokinetic profile is the target profile of all controlled

release dosage forms to ensure that the controlled release dosage form has similar efficacy to multiple dosings of the immediate release dosage form. (5/14/2014 Tr. 577:11-15.) In addition, the use of gabapentin in Depomed's WO '107 dosage form, would have been obvious to one of skill in the art as previously discussed for the '927 and '756 Patents. (See *supra*, ¶¶ 141-176.)

209. Dr. Flanagan testified that all controlled release formulations are designed to meet the limitations of: "released at a rate sufficient to achieve lower maximum plasma concentration" and "without loss on bio-availability as compared to an immediate-release formulation." (5/15/2014 Tr. 608:20-609:10.) He explained that these are the natural parameters that are achieved for controlled release dosage forms and, in fact, these claimed parameters are the very concept of a controlled release formulation. (Id. at 609:8-610:1.) Even Depomed's Dr. Derendorf testified that a controlled release drug would release the drug slower (5/13/2014 Tr. 362:16-18), resulting in a lower C_{max} (id. at 364:23-365:3) and a longer T_{max}. (Id. at 365:16-21.)

210. For these reasons, and the reasons discussed above with respect to the '927, '989 and '756 Patents, independent claims 1, 12, 22 and 24 of the '332 Patent and claims 1 and 22 of the '992 Patent would have been obvious to one of ordinary skill in the art over Depomed's WO '107 in view of Rowbotham. (5/15/2014 Tr. 624:3-17, 625:1-8.)

b) Independent Claims 1, 12, 22 and 24 of the '332 Patent and Claims 1 and 22 of the '992 Patent Would Have Been Obvious in View of WO '128 and Rowbotham.

211. WO '128 and Rowbotham together disclose all the limitations of independent claims 1, 12, 22 and 24 of the '332 Patent and 1 and 22 of the '992 Patent except for the specific pharmacokinetic parameters of gabapentin.

212. Dr. Flanagan testified that Rowbotham discloses gabapentin was known to be an effective treatment of neuropathic pain, with daily doses ranging from 300 mg/day to

3,600 mg/day. (5/14/2014 Tr. 559:4-560:5; 5/15/2014 Tr. 622:17-623:3; DTX 313 at GRALISE_JDG_00000452.)

213. WO '128 discloses "a new dosage form for highly soluble medicaments . . . and it provides controlled release of the drug for prolonged gastric residence, which enables efficient delivery of the drug or drugs normally absorbed in the upper GI tract. . . . And also it indicates an approach using size to modulate or control gastric residence." (5/15/2014 Tr. 626:4-11, 704:13-705:4, 713:22-714:17; DTX 236 at GRALISE_JDG_00000057.) As Dr. Flanagan testified, the size of the dosage form of WO '128 was designed to be "convenient for administration to humans" and can then imbibe fluid and swell "over a short period of time to a size that will encourage prolonged gastric residence and allow sustained delivery of the drug to absorption sites in the upper gastrointestinal tract." (5/15/2014 Tr. 626:12-20; DTX 236 at GRALISE_JDG_00000062.) As explained by Dr. Flanagan, the dosage form of WO '128 is drawn for "a drug with high water solubility and limited window of absorption, such where the window is in the upper gastrointestinal tract. So the dosage form has prolonged gastric residence to release the drug into that window of absorption." (5/15/2014 Tr. 626:22-627:1; see also 5/15/2014 Tr. 713:22-714:17; DTX 236 at GRALISE_JDG_00000070.)

214. WO '128 discloses that "oral controlled release delivery systems function by releasing their payload of drug over an extended period of time following administration." (DTX 236 at GRALISE_JDG_00000058.) As Dr. Flanagan stated, WO '128 also describes the release of metformin for over ten hours by diffusion while being gastric retained. (5/15/2014 Tr. 627:14-21.)

215. The specification goes on to explain that very soluble drugs can be controlled by reducing their rate of dissolution by "embedding the drug in a polymeric matrix or surrounding it

with a polymeric barrier membrane through which drug must diffuse to be released for absorption." (DTX 236 at GRALISE_JDG_00000059.) WO '128 further provides that, "[i]n a controlled release dosage form, the formulator tries to reduce the rate of dissolution by, for example, embedding the drug in a polymeric matrix . . . through which the drug must diffuse to be released for absorption." (Id. at GRALISE_JDG_00000059.)

216. WO '128 further provides that it has two benefits: "(a) [it] achieves extended gastric residence by virtue of size but will degrade in vivo so as not to have potential for causing gastric or intestinal obstruction, and (b) [it] controls drug release adequately where the initial burst of drug is under control." (Id. at GRALISE_JDG_00000070.) The formulation "can be administered to various mammalian species, such as dogs, cats, humans, etc., in need of such treatment." (Id. at GRALISE_JDG_00000082-83.)

217. As both Drs. Flanagan and Mayersohn testified, WO '128 further shows that administration of a controlled release dosage form (denoted Example 3) to subjects resulted in a lower C_{max}, a longer T_{max}, and an equivalent AUC_{inf} of the drug in comparison to an immediate release dosage form (denoted Glucophage). (5/15/2014 Tr. 627:2-7, 699:15-701:4; DTX 236 at GRALISE_JDG-00000090 (Example 5).) In any event, as Dr. Flanagan testified, these pharmacokinetic properties are nothing more than the routine targets that those of ordinary skill in the art target in making a controlled release pharmaceutical product. (5/14/2014 Tr. 573:19-23; 5/15/2014 Tr. 609:23-610:1, 614:11-14, 616:11-15, 696:17-697:2.) Even Depomed's Dr. Derendorf testified that a controlled release drug would release the drug slower (5/13/2014 Tr. 362:16-18), resulting in a lower C_{max} (id. at 364:23-365:3) and a longer T_{max}. (Id. at 365:16-21.) It would have been a routine matter for formulators of ordinary skill in the art to adjust the

release rate of drug to obtain these routine and standard pharmacokinetic parameters. (See *supra*, ¶¶ 192-194.)

218. All of the experts agree that one of ordinary skill in the art in 2001 would have been motivated to make a controlled release gabapentin formulation to alleviate the burden on patients to take multiple doses per day, improve patient compliance, and reduce the incidence of side effects. (5/15/2014 Tr. 751:11-18; 5/19/2014 Tr. 963:21-964:1; 5/14/2014 Tr. 558:5-559:3; 5/16/2014 Tr. 873:12-22; DTX 267 at GRALISE_JDG_00000130.) All of the experts agreed that the most obvious platform to try would be a gastric retained dosage form – and WO '128 is an example of a gastric retained dosage form. (5/15/2014 Tr. 637:2-6, 702:4-16, 713:22-714:17, 769:24-770:3; 5/19/2014 Tr. 964:15-965:15.) WO '128 states that any number of water soluble drugs (with significantly different chemical and physiological properties) can be formulated into the WO '128 dosage form, including CNS agents – and gabapentin is a CNS agent. (DTX 236 at GRALISE_JDG_00000080.) Furthermore, Drs. Flanagan and Mayersohn testified that the WO '128 dosage form would be useful for drugs having three critical properties: (1) high water solubility; (2) saturable absorption; and (3) a window of absorption high in the gastrointestinal tract. (5/15/2014 Tr. 563:19-24; 5/15/2014 Tr. 698:17-20.) It was well known in the art that gabapentin had all three of these properties (5/14/2014 Tr. 560:6-561:9, 564:22-565:1; 5/15/2014 Tr. 686:1-5; PTX 500 at GRALISE_JDG_00000601, 603; DTX 267 at GRALISE_JDG_00000127), and would thus have benefited from being formulated in the WO '128 dosage form.

219. Although WO '128 does not provide pharmacokinetic information for gabapentin, Dr. Mayersohn testified that a person of ordinary skill in the art would have a reasonable expectation of achieving a similar effect on the pharmacokinetics of gabapentin by putting

gabapentin into the WO '128 dosage form – i.e., reduced C_{max}, longer T_{max} and similar $AUC_{infinity}$ compared to the immediate-release product. (5/15/2014 Tr. 705:19-706:1, 715:21-717:18, 718:16-21; 717:22-718:11.) Dr. Mayersohn explained that the reasonable expectation of success was based upon the similar properties that both gabapentin and metformin were known to have in common. (Id. at 718:3.) These common properties are high water solubility, saturable absorption, and a limited window of absorption high in the gastrointestinal tract. (5/15/2014 Tr. 563:19-24; 5/15/2014 Tr. 698:17-20.) Because both metformin and gabapentin are similar in these properties, Dr. Mayersohn testified that one of ordinary skill in the art would have reasonably expected that their behavior would be the same when put into the WO '128 dosage form. (5/15/2014 Tr. 715:21-717:18; see also Dr. Flanagan, 5/15/2014 Tr. 626:4-628:18, 628:20-22.)

220. For these reasons, claims 1, 12, 22 and 24 of the '332 Patent and claims 1 and 22 of the '992 Patent would have been obvious to one of ordinary skill in the art over WO '128 in view of Rowbotham. (5/15/2014 Tr. 627:22-628:2.)

c) Dependent Claims 6 and 17 of the '332 Patent and Claim 5 of the '992 Patent Would Have Been Obvious In View of Rowbotham and Depomed's WO '107 or WO '128.

221. Depomed asserts two additional claims of the '332 Patent, claims 6 and 17. (Stip. Fact ¶ 89.) Claim 6 depends from claims 1, 4 and 5, which add the following limitations: (a) "wherein the matrix is a polymer matrix" (claim 4); (b) "wherein the polymer matrix is comprised of a swellable, hydrophilic polymer" (claim 5); and (c) "wherein the gabapentin is released from the polymer matrix by diffusion" (claim 6). (Stip. Fact ¶¶ 92-94; JTX 6.) Claim 17 depends from claim 12 of the '332 Patent, and requires that the condition being treated is neuropathic pain. (Stip. Fact ¶ 96; JTX 6.)

222. Depomed also asserts one additional claim of the '992 Patent, claim 5. (Stip. Fact ¶ 100.) Claim 5 depends from claim 4, which in turn depends from claim 1. Claims 4 and 5 add the following limitations: (a) "wherein the matrix is a polymer matrix" (claim 4); and (b) "wherein the polymer matrix is comprised of a swellable, hydrophilic polymer" (claim 5). (Stip. Fact ¶¶ 101, 103-104; JTX 7.)

223. With respect to claim 4 of the '332 Patent and claim 4 of the '992 Patent, WO '128 discloses hydrophilic polymers used as a matrix in the formulations. (5/15/2014 Tr. 699:15-700:3; DTX 236 at GRALISE_JDG_00000070-71, 73.) Similarly, Dr. Flanagan testified Depomed's WO '107 discloses that "the drug is dispersed in a polymeric matrix." (5/14/2014 Tr. 556:22-557:8; DTX 234 at GRALISE_JDG_00000844.) Accordingly, claim 4 of the '332 Patent and claim 4 of the '992 Patent would have been obvious over the same prior art discussed above with respect to claim 1 of the '332 Patent and claim 1 of the '992 Patent. (5/15/2014 Tr. 626:4-628:18, 628:20-22.)

224. With respect to claim 5 of the '332 Patent and claim 5 of the '992 Patent, WO '128 discloses that its dosage form is a swellable, hydrophilic polymer matrix. (DTX 236 at GRALISE_JDG_00000086 (the dosage form "following ingestion would remain (or swell to, by hydration of the polymers used in the fabrication of the tablet) a size that does not easily pass through the pylorus (15mm or greater) when taken with a meal.").) Similarly, Depomed's WO '107 discloses that "the drug is dispersed in a polymeric matrix that is water swellable rather than merely hydrophilic." (DTX 234 at GRALISE_JDG_00000844.) Accordingly, claim 5 of the '332 Patent and claim 5 of the '992 Patent would have been obvious over the same prior art discussed above with respect to claims 1 and 4 of the '332 Patent and claims 1 and 4 of the '992 Patent. (5/15/2014 Tr. 626:4-628:18, 628:20-22.)

225. With respect to claim 6 of the '332 Patent, WO '128 discloses that the dosage form releases the drug by diffusion. (DTX 236 at GRALISE_JDG_00000071 ("Drug upon being released from the particles of the inner phase, in effect, migrates through the outer solid continuous phase and then is released from the formulation into the upper gastrointestinal tract to be available for absorption.").) Similarly, Depomed's WO '107 discloses that "the penetrating fluid then causes release of the drug in a gradual and prolonged manner by the process of solution diffusion" with the "rate-limiting factor in the release of the drug [being] controlled diffusion of the drug from the matrix." (DTX 234 at GRALISE_JDG_00000844-45.) Accordingly, claim 6 of the '332 Patent would have been obvious over the same prior art discussed above with respect to claims 1, 4 and 5 of the '332 Patent. (5/15/2014 Tr. 626:4-628:18, 628:20-22.)

226. With respect to claim 17 of the '332 Patent, one of ordinary skill in the art in October 2001 knew that gabapentin was used to treat neuropathic pain. (5/16/2014 Tr. 857:3-8; see DTX 313.) For example, Rowbotham disclosed the use of gabapentin for neuropathic pain. (5/14/2014 Tr. 559:4-560:5; 5/15/2014 Tr. 622:17-623:3; DTX 313 at GRALISE_JDG_00000451-452.) The use of gabapentin is merely the use of a known drug for its known purpose – i.e., as a treatment of neuropathic pain. Thus, claim 17 of the '332 Patent would have been obvious over the same prior art discussed above with respect to claim 12 of the '332 Patent. (5/15/2014 Tr. 626:4-628:18, 628:20-22.)

227. For these reasons, claims 6 and 17 of the '332 Patent and claim 5 of the '992 Patent would have been obvious to one of ordinary skill in the art over Rowbotham in view of Depomed's WO '107 or WO '128.

5. Depomed's Evidence of Secondary Considerations Does Not Outweigh the Strong Showing of Obviousness.

a) No Skepticism or Failure of Others

228. Depomed alleges that three different pharmaceutical companies, Warner-Lambert, Andrx and XenoPort, tried and failed to formulate a controlled release gabapentin product, and expressed skepticism regarding their ability to do so.

229. Dr. Bockbrader, a former Warner-Lambert employee for 30 years (5/15/2014 Tr. 744:24-25), testified that Warner-Lambert, in the mid-1980s, attempted to make a controlled release formulation of gabapentin. (Id. at 767:16-20.) The Warner-Lambert attempt used a traditional controlled release formulation which would have released the drug throughout the gastrointestinal tract. (Id. at 767:25-768:6.) After this attempt in the mid-80s, Warner-Lambert did not attempt to develop another controlled release formulation of gabapentin. (Id. 760:9-11.)

230. This attempt by Warner-Lambert to make a controlled release formulation of gabapentin occurred at a time before it was known that gabapentin was absorbed high in the gastrointestinal tract and/or that gabapentin was absorbed through saturable transporters. (Id. at 768:7-21, 770:15-771:4, 768:22-770:3.) In fact, the study of this formulation led, in part, to the knowledge that gabapentin had a narrow window of absorption in the upper gastrointestinal tract. (5/15/2014 Tr. 768:9-21.) Dr. Bockbrader testified that one of ordinary skill would not have used this traditional sustained-release formulation after learning of gabapentin's limited absorption high in the gastrointestinal tract through saturable transporters. (Id. at 769:24-770:3; 759:21-25.) Thus, the attempt by Warner-Lambert to make a controlled release formulation of gabapentin via conventional formulations cannot be said to have failed because it was attempted at a time well before Depomed's WO '107 or WO '128 came into the public domain and itself led to the knowledge that gabapentin would require a gastric retained dosage form.

231. Warner-Lambert then met once with a French company that had a gastric retained formulation in 1995, but that dosage form only remained in the stomach for six hours in the fed mode. (Id. at 756:19-757:9.) And Dr. Bockbrader admitted that Warner-Lambert's interest in the French Company was that their formulation was suggested to work in fasted mode. This particular characteristic was desirable as Neurontin could be taken with or without food. (5/15/2014 Tr. 772:15-24.) Warner-Lambert, however, only met with the French company once in 1995 after Neurontin had been approved for epilepsy, but before Neurontin had reached its blockbuster status. (Id. at 771:5-13, 772:6-8.) Furthermore, these discussions involved preliminary discussions about the potential of jointly developing a variety of drug products, rather than an effort specifically targeted at formulating gabapentin. Thus, it cannot be said Warner-Lambert's meeting with this French company even constitutes an "attempt" to make a gastric-retained dosage form containing gabapentin, and the meeting also occurred before the relevant prior art Depomed's WO '107 or WO '128 came into the public domain. Furthermore, while the French company expressed some skepticism about their dosage form reliably staying in the stomach, Depomed's WO '107 and WO '128 expresses no such doubts.

232. Warner-Lambert also met with ALZA about a controlled release formulation, but that formulation was not designed to be gastric retained. (Id. at 764:2-13, 775:1-10.) Dr. Bockbrader admitted that ALZA's formulation was a rigid osmotic pump that does not provide gastric retention. (5/15/2014 Tr. 774:22-775:10.) Furthermore, Dr. Bockbrader testified that the meeting with ALZA lasted for only about an hour in 1995 without any follow-up. (Id. at 774:14-19.) In fact, ALZA had set up many meetings with Warner-Lambert to discuss many potential joint development projects. (Id. at 775:14-19.) Thus, like with the French company, there was no attempt to actually formulate a gastric retained gabapentin product.

Furthermore, Dr. Bockbrader explained that one of ordinary skill would have known that a sustained-release formulation that was not gastric retained would not have worked for gabapentin. (Id. at 769:24-770:3; 759:21-25.) Thus, the meeting Warner-Lambert and ALZA is not probative of skepticism or failure of others to make a gastric retained gabapentin formulation.

233. Lyrica, another Pfizer product containing the active agent pregabalin, is also indicated for the treatment of post-herpetic neuralgia (among other things) and thus competes directly with Gralise and other gabapentin products. (5/15/2014 Tr. 765:22-766:2.) Lyrica, like Neurontin, is an immediate release product that is taken two or three times per day. (Id. at 765:20-21.) It is notable that ten years after the launch of Lyrica, Pfizer still has not marketed a controlled release version of Lyrica. (Id. at 766:3-6.) This suggests that Warner-Lambert's failure to develop an extended-release gabapentin product may be a result of a business strategy rather than a technical inability to formulate one.

234. Dr. Felton also suggested that Andrx unsuccessfully attempted to make a controlled release formulation of gabapentin. (5/19/2014 Tr. 1001:23-25, 1002:22-1005:10.) The formulations, however, were not designed to be gastric retained, as Dr. Felton admitted. (Id. at 1017:23-1018:10, 1019:12-1020:6.) Dr. Felton further admitted that Andrx knew gabapentin was absorbed in the upper gastrointestinal tract and that it would not have made sense to make a controlled release formulation of gabapentin that released the drug throughout the gastrointestinal tract. (5/19/2014 Tr. 1017:23-1018:10, 1021:8-15.) Furthermore, the same formulations were also used to test delivery of Andrx's proprietary gabapentanoid pro-drug, which has a different absorption profile than gabapentin not limited to the upper gastrointestinal tract. (Id. at 1019:12-1020:6.) Dr. Felton never considered whether Andrx was merely using the

gabapentin formulations as controls for the formulations containing their proprietary prodrug. (Id. at 1020:21-1021:7.) Thus, it is more likely Andrx was using the gabapentin formulations as a baseline to compare with their proprietary gabapentanoid pro-drug, and, as such, cannot be considered an actual attempt at making a controlled release formulation of gabapentin itself.

235. Dr. Gidal similarly suggested XenoPort was skeptical of a controlled release gabapentin formulation when they decided to develop a prodrug of gabapentin. (5/16/2014 Tr. 849:3-7, 853:12-16; PTX 269 at DEPOACT0958153; PTX 277 at DEPOACT0970277.) Dr. Gidal testified, however, that he was never asked to help develop a controlled release form of gabapentin for XenoPort and that they only approached him to develop a pro-drug. (5/16/2014 Tr. 860:6-15, 861:14-16.) In fact, XenoPort's business was to apply to develop new compounds by its prodrug technology to existing drugs. (PTX 277 at DEPOACT0970277; 5/16/2014 Tr. 861:5-16.) Little can be inferred from Dr. Gidal's testimony on this point because XenoPort's desire for a novel prodrug hardly constitutes skepticism of the ability to make a controlled release formulation of gabapentin.

236. For these reasons, Depomed has not demonstrated that there was skepticism in the art or that others had tried and failed to make a gastric retained gabapentin dosage form.

b) No Long-felt But Unmet Need

237. Dr. Brown suggested there was a long felt need for once-daily formulation of gabapentin as described in the patented claims at the time of the patent application. (5/16/2014 Tr. 870:3-13.) Dr. Brown's testimony is entitled to little weight, as she admitted that she works for Depomed as a member of its speaker's bureau for Gralise and does not consider herself one of ordinary skill in the art. (Id. at 884:12-22, 869:4-9.)

238. Furthermore, Dr. Brown testified that this alleged long-felt need was not met until Gralise was launched in 2011, a decade after Depomed filed its application for the Gabapentin

Patents. Dr. Brown also admitted that she did not consider whether the prior art would have met any need that existed at an earlier point in time. (Id. at 889:21-25.) Thus, Dr. Brown's testimony is not probative of a long-felt but unmet need for the subject matter claimed in the Gabapentin Patents.

239. Furthermore, Dr. Brown admitted that she prescribes Lyrica, another immediate release product that is administered multiple times daily, to patients more often than Gralise if an immediate release gabapentin is not successful. (Id. at 887:14-20.) This tends to show that the need for a once-daily dose of gabapentin was not very acute.

240. Dr. Sinatra testified that in his medical experience there are no compliance problems with taking immediate release gabapentin because, unlike medications used for treating undetectable symptoms such as high blood pressure, a patient being treated for pain would not forget to take their pain medication. (5/16/2014 Tr. 903:17-904:9.)

241. [redacted]

242. On balance, while there may be some evidence of a need for a once-daily dosing regimen of gabapentin that was not met until Gralise was launched in 2011, this evidence is very weak evidence that is linked tenuously at best to the Gabapentin Patents.

c) No Copying

243. Depomed presented no expert testimony on copying of the Gabapentin Patents by Actavis. The fact witnesses Depomed presented were all Actavis employees. None of their testimony established that Actavis copied the Patents-In-Suit.

244. Dr. Hejazi testified that Actavis' formulation was not designed to be gastric retained and was not designed to have a specific size in the stomach. (5/12/2014 Tr. 82:3-8.)

Dr. Hejazi also explained that certain excipients, like the matrix polymers, were chosen for Actavis' ANDA Products because of Actavis' prior experience in using those excipients and because of the known controlled release properties of those excipients. (Id. at 81:21-82:2.)

245. Dr. Johnson testified that Actavis' gabapentin once daily project was of high importance due to the possibility of receiving marketing exclusivity from FDA by being the first to file. (5/20/2014 Tr. 1143:7-10, 1146:2-11.) Because it was a first to file opportunity, Actavis performed required dissolution testing in a short time period in order to be a first filer. (Id. at 1148:13-1149:2.) This meant some people worked on the weekends (id. at 1158:25-1159:6), but that weekend work was not unusual at Actavis. (Id. at 1159:8-9.) In fact, as Dr. Venugopal explained, "about 30 to 40 percent of the projects that we worked on [at Actavis] w[ere] first-to-file opportunities" and these first to file projects had higher priorities compared to non-first to file projects. (5/13/2014 Tr. 329:23-330:9.)

246. Dr. Venugopal also testified that using multiple contract research organizations was not unusual for first to file projects (5/13/2014 Tr. 331:1-13) since all first-to-file projects were considered high priority projects at Actavis. (Id. at 330:23-25.) Thus, the extra work put in by Actavis and its employees on gabapentin once-daily was not unusual or extraordinary in comparison to other first-to-file opportunities. Accordingly, Depomed has not adduced evidence of copying by Actavis.

d) No Commercial Success

247. [redacted]

[redacted]

248. [redacted]

249. [redacted]

250. [redacted]

[redacted]

251. [redacted]

[redacted]

252. [redacted]

[redacted]

253. [redacted]

254. [redacted]

VI. THE ASSERTED CLAIMS OF THE '962 PATENT ARE INVALID AS OBVIOUS

A. Depomed's WO '107 Teaches or Suggests All of the Limitations of the Asserted '962 Patent Claims.

255. The asserted claims of the '962 Patent, claims 5, 8, 10 and 13, would have been obvious to one of ordinary skill over Depomed's WO '107 along with the knowledge of a person of ordinary skill in the art. (D.I. 327 at 14-15; Stip. Fact ¶ 51.)

256. Dr. Flanagan described Depomed's WO '107 as disclosing or suggesting each and every limitation of claim 1 of the '962 Patent. Depomed's WO '107 discloses a dosage form that "relates in particular to drug delivery systems that are retained in the stomach for an extended period of time while releasing a highly soluble drug in a controlled manner of an extended period of time." (5/14/2014 Tr. 556:4-12; DTX 234 at GRALISE_JDG_00000843.) The dosage form of Depomed's WO '107 is "a formulation in which the drug is dispersed in a polymeric matrix that is water-swellable rather than merely hydrophilic, and that erodes at a rate that is substantially less than its swelling rate." (Id. at GRALISE_JDG_00000844.) This swelling polymeric matrix, as explained by Dr. Flanagan, "(i) swells . . . to a size large enough to cause it

to be retained in the stomach during the fed mode, and (ii) it retards the rate of diffusion of a highly soluble drug long enough to provide multi-hour, controlled delivery of the drug into the stomach." (5/14/2014 Tr. 556:4-12; DTX 234 at GRALISE_JDG_00000845.) In fact, Dr. Flanagan explained that the polymers in the matrix swell to several times their original volume and the dosage form swells to at least twice its original size upon ingestion. (5/14/2014 Tr. 631:15-632:3.)

257. Depomed's WO '107 further explains that the dosage form contains a monolithic matrix. Depomed's WO '107 explains that, when "the formulation is a tablet or capsule, the dosage form is usually one such tablet or capsule." (DTX 234 at GRALISE_JDG_00000850.) The Examples describe the formation of pellets and tablets by simply compressing mixtures of drug, polymer and magnesium stearate. (Id. at GRALISE_JDG_00000851 ("Drug and polymer . . . were compressed into pellets . . . ."), GRALISE_JDG_00000853 ("Each formulation was compressed into a tablet.").) These are common methods that are known in the art to make a monolithic polymeric matrix containing a drug.

258. Dr. Flanagan describes the dosage forms of Depomed's WO '107. (5/15/2014 Tr. 630:14-25.) They are non-circular in shape, having dimensions of an "elongated tablet with dimensions 18 to 22 mm in length, 6.5 to 7.8 mm in width, and 6.2 to 7.5 mm in height," and have a "preferred set of dimensions is 20 mm in length, 6.7 mm in width, and 6.4 mm in height." (Id.; DTX 234 at GRALISE_JDG_00000849.) The ranges specified for each dimension are not equal – disclosing to one of ordinary skill in the art that none of the three dimensions should be identical. Furthermore, the maximum dimension is 22 mm or 2.2 cm, which is shorter than 3.0 cm. Therefore, Depomed's WO '107 discloses a dosage form that is "non-circular with first and second orthogonal axes of unequal length," and the "longer such axis having a maximum

length of 3.0 cm when said matrix is unswollen." (JTX 1 at claim 1.) In any event, setting a maximum unswollen dimension of 3.0 cm for an oral dosage form is nothing more than common sense because a tablet, as Dr. Flanagan explained, that exceeds this size (about 1.2 inches) would be very uncomfortable (and nearly impossible for many people) to swallow. (5/15/2014 Tr. 623:4-13.)

259. Although Depomed's WO '107 does not specifically disclose an oval tablet, it further states that an elongated tablet, as described in its examples, is not the only shape that this dosage form can take. (DTX 234 at GRALISE_JDG_00000849 ("These are merely examples; the shapes and sizes can be varied considerably.").) Oval tablets had been routinely used in the prior art. (5/15/2014 Tr. 634:20-635:3.) For example, WO '360 discloses a "pharmaceutical formulation in a generally oval shape including, but not limited to, oval, modified oval and caplet-shaped form." (DTX 235 at GRALISE_JDG-00000653.) Furthermore, publications such as the TABLETING SPECIFICATION MANUAL demonstrate that oval shapes are a common tablet shape. (DTX 39 at ACTGAB000321919 (Fig. 25).) In fact, punches for oval shaped tablets are commercially available from, e.g., the Elizabeth Tool and Die Co. (See 5/14/2014 Tr. 475:3-18, 476:1-18; 490:12-19.)

260. Dr. Flanagan testified that creating a gastric retained dosage form of a specific swollen size, i.e. one large enough to remain in the stomach during fed mode, would be well within the purview of the knowledge of one skilled in the art with routine testing. (5/15/2014 Tr. 632:11-16, 633:3-7.) The types of sizes that would be gastric retained because they resist expulsion from the stomach were well known in the art. For example, WO '128 explains that "where Caldwell describes a device that when it reaches the stomach, it becomes a minimum size of 1.6 centimeters and it can have a maximum size of five centimeters so it will not pass from the

stomach through the pylorus." (Id. at 632:17-23.) Thus, those of ordinary skill in the art would understand that the dosage form should be dimensioned and swellable polymers should be selected such that the swollen tablet would reach a minimum size of, e.g., 1.2 cm quickly to avoid passing from the stomach through the pylorus.

261. The shape of the tablet and the various dimensions set forth in the '962 Patent would have been obvious design choices to one of skill in the art. (5/15/2014 Tr. 633:13-634:4.) Dr. Flanagan testified that it is "very common for one skilled in the art to be selecting different sizes and shapes of tablets, so [shape] would be just a design choice." (Id.)

262. For these reasons, claim 1of the '962 Patent would have been obvious to one of ordinary skill in the art over WO '107. (5/15/2014 Tr. 630:3-6, 635:7-14.)

263. The four asserted claims of the '962 Patent, claims 5, 8, 10 and 13, all depend directly or indirectly from independent claim 1. Thus, the discussion with respect to the obviousness of claim 1 is equally applicable.

264. Dependent claim 5 incorporates all of the limitations of claim 1 with the further limitation that the shorter axis has a "length of 0.7 cm to 1.5 cm when said matrix is unswollen." (JTX 1 at claim 5.) The limited dimensions of claim 5 are within the disclosures of Depomed's WO '107 and are routine design choices for one of ordinary skill. Depomed's WO '107 discloses preferred dimensions of an elongated tablet before ingestion to be "18 to 22 mm in length, 6.5 to 7.8 mm in width, and 6.2 to 7.5 mm in height." (5/15/2014 Tr. 630:14-25; DTX 234 at GRALISE_JDG_00000849.) Depomed's WO '107 states that the dosage form can be between 6.2 to 7.5 mm, a range that overlaps with the claimed lengths. Further, Dr. Flanagan testified that it would have been nothing more than an obvious design choice for one of skill in the art to dimension the unswollen tablet as large as possible to decrease the likelihood it will be

expelled through the pylorus before it swells, ensuring that it is small enough to comfortably swallow. (5/15/2014 Tr. 626:10-20.) For these reasons and the reasons discussed above with respect to claim 1, claim 5 would have been obvious to one of ordinary skill in the art over the prior art. (5/15/2014 Tr. 635:15-21.)

265. Dependent claim 8 incorporates all the limitations of claim 1 with the additional limitation that the longer axis of the dosage form has a "maximum length of 2.5 cm when said matrix is unswollen." (JTX 1 at claim 8.) As recited by Dr. Flanagan, Depomed's WO '107 discloses the dimension of an elongated tablet before ingestion to be "18 to 22 mm in length, 6.5 to 7.8 mm in width, and 6.2 to 7.5 mm in height." (5/15/2014 Tr. 630:14-25; DTX 234 at GRALISE_JDG_00000849.) The longest dimension of Depomed's WO '107 tablet in the unswollen state is thus 22 mm and is thus shorter than the 2.5 cm maximum length specified by claim 8 of the '962 Patent. In any event, as Dr. Flanagan explained, setting a maximum unswollen dimension of 2.5 cm is nothing more than common sense because a tablet that exceeds this size (about 1 inch) would be very uncomfortable (and nearly impossible for many people) to swallow. (5/15/2014 Tr. 623:4-13.) And, this would also have been an obvious design choice for one of skill in the art. (5/15/2014 Tr. 633:13-634:4.) Accordingly, claim 8 of the '962 Patent would have been obvious for these reasons, as well as the reasons discussed above with respect to claim 1. (5/15/2014 Tr. 635:15-21.)

266. Dependent claim 10 of the '962 Patent incorporates all of the limitations of claim 1 with the additional limitation that the "matrix is a water-swellable polymer." (JTX 1 at claim 10.) Depomed's WO '107 discloses a drug dispersed in a polymeric matrix that is water swellable, where the drug is released by diffusion and where the polymers in the matrix swell upon ingestion, which promotes gastric retention of the dosage form during the fed mode.

(5/14/2014 Tr. 556:22-557:8; 5/15/2014 Tr. 631:9-23, 683:5-13; DTX 234 at GRALISE_JDG_00000844.) Depomed's WO '107 states that the "matrix . . . swells upon ingestion to achieve a size that is at least about twice its unswelled volume and that promotes gastric retention during the fed mode." (DTX 234 at GRALISE_JDG_00000844.) Dr. Flanagan explained that the polymers disclosed in Depomed's WO '107 "are all hydrophilic and they also all swell to many times their original volume." (5/15/2014 Tr. 632:2-3.) Accordingly, claim 10 of the '962 Patent would have been obvious for these reasons, as well as the reasons discussed above with respect to claim 1. (5/15/2014 Tr. 635:15-21.)

267. Dependent claim 13 of the '962 Patent incorporates all of the limitations of claim 10 with the additional limitation that the water-swellable polymer in the dosage form is a "member selected from the group consisting of poly(ethylene oxide), hydroxypropylmethyl cellulose, and hydroxyethyl cellulose." (JTX 1 at claim 13.) Depomed's WO '107 states that "examples of polymers suitable for use in this invention are cellulose polymers and their derivatives . . . particularly preferred alkyl-substituted celluloses are hydroxyethylcellulose and hydroxypropylmethylcellulose . . . . A particularly preferred polyalklyene oxide is poly(ethylene oxide)." (5/15/2014 Tr. 632:2-3; DTX 234 at GRALISE_JDG_00000847.) That these polymers were well-known to those of ordinary skill in the art, as described above, would make them an obvious starting point for the formulations. Because Depomed's WO '107 discloses the limitations of claim 13, dependent claim 13 thus would have been obvious to one of ordinary skill in the art over the prior art as described above with respect to claim 1. (5/15/2014 Tr. 635:15-21.)

268. For these reasons, claims 5, 8, 10 and 13of the '962 Patent would have been obvious to one of ordinary skill in the art over WO '107. (5/15/2014 Tr. 635:15-21.)

B. Secondary Considerations Do Not Outweigh the Obviousness of the Asserted Claims of the '962 Patent.

269. Depomed presented evidence concerning only two of the secondary considerations with respect to the '962 Patent: (1) long-felt but unmet need; and (2) commercial success.

270. Depomed failed to demonstrate that the '962 Patent met a long-felt need. Dr. Hopfenberg testified that the key improvements of the '962 Patent over the '475 and '280 Patents was the claimed dosage forms ability to swell to a minimum length of 1.2 cm within one hour of immersion and that its shape when projected be either an oval or parallelogram. (5/19/2014 Tr. 934:10-935:20, 938:2-19.) He nevertheless went on to testify that even as of 2012 there continued to be a long felt need for improved, gastric retained dosage forms. (Id. at 949:17-950:1.) Therefore, if there even was such a long-felt need, the '962 Patent failed to meet such a need.

271. With respect to its allegations of commercial success, as explained above, the modest sales of Gralise are not evidence of commercial success of the subject matter claimed in the '962 Patent, when considered in the context of Gralise's speculative profitability even ten years in the future, the miniscule share of the gabapentinoid market that Gralise has secured, Depomed's significant marketing efforts and Depomed's other patents covering Gralise.

272. [redacted]

[redacted]

273. For these reasons, Depomed has failed to adduce evidence of secondary considerations sufficient to overcome the strong showing of obviousness made by Actavis.

VII. THE ASSERTED CLAIMS OF THE '280 PATENT ARE INVALID AS INDEFINITE.

274. The asserted claims of the '280 Patent are invalid as indefinite. Claim 1 recites that the claimed dosage form must swell to a "size exceeding the pyloric diameter in the fed mode." (Stip. Fact ¶ 53, JTX 2.) All other asserted claims of the '280 Patent depend from claim 1 and thus also include this limitation.

275. As Dr. Annunziata explained, the pylorus is the structure in the stomach that regulates materials leaving the stomach into the intestine. (5/12/2014 Tr. 152:16-153:1.) In the fed mode, the pylorus is generally, tightly clenched closed in order to prevent food from moving into the intestine before it is broken down into small particles. (Id. at 152:19-23.) Periodically, the pylorus relaxes and opens, allowing some of the stomach contents (including larger particles of food and other matter) to pass from the stomach into the intestine. (5/13/2014 Tr. 235:9-19.)

276. The reference to "pyloric diameter in the fed mode" in the '280 Patent claims does not explicitly state whether it refers to the pyloric diameter when the pylorus is tightly clenched (i.e., essentially zero) or during the moments during which the pylorus is momentarily relaxed. Dr. Annunziata explained that when the pylorus is tightly clenched, as it would be in fed mode, just about any dosage form would be larger than the pyloric diameter, even without swelling. (5/13/2014 Tr. 221:21-25, 253:22-254:4.) Because the claims refer to the tablet

swelling to a size that exceeds the pyloric diameter, however, the "pyloric diameter" in the claims must refer to the periods when the pylorus is relaxed.

277. Depomed's own experts admit that there is no generally-applicable size for the pyloric diameter in the fed mode, as it is dependent on a multitude of factors. For instance, Dr. Annunziata testified that the pyloric diameter during the fed mode is highly variable and that it's not possible to know what its size is in any given patient or at any given time. (5/13/2014 Tr. 244:12-15; 245:25-246:22.) He explained that the pyloric diameter is "definitely variable as everybody, every person is variable, in size, shape, et cetera." (5/13/2014 Tr. 244:12-15; 245:25-246:22.) Dr. Flanagan similarly explained that there is no specific size in the art relating to improving gastric retention of a dosage form given the uncertainty and variability between people. (5/15/2014 Tr. 632:11-16.)

278. In fact, the most precise data regarding the pyloric diameter in the fed mode was published by Timmermans. In Timmermans, which Dr. Annunziata relied on, the reported pyloric diameter was 12.8 mm ± 7.0 mm. (5/13/2014 Tr. 244:16-19; PTX245 at DEPOACT0114761.) Thus, the only reasonable scientific conclusion is that the pyloric diameter is somewhere between 5.8 mm and 19.8 mm. This wide range fails to provide those of ordinary skill in the art any guidance as to whether or not a tablet that swells to a size within the range exceeds the size of the pyloric diameter.

279. Because of this variability, Dr. Annunziata testified that he could not say with reasonable scientific certainty whether 12 millimeters or even 20 millimeters exceeds the size of the pyloric diameter. (5/13/2014 Tr. 244:12-15, 245:25-246:22, 249:16-21, 249:22-250:13, 252:19-22.)

280. Because even an expert in gastrointestinal physiology could not reasonably state what a size that exceeds the pyloric diameter in the fed mode is, claim 1 of the '280 Patent fails to reasonably apprise those of skill in the art of the scope of the claim.

VIII. NONINFRINGEMENT

A. The Gabapentin Patents

1. Depomed has Failed to Prove that Actavis' ANDA Products "Swell . . . to Increase its Size to Promote Gastric Retention of the Dosage Form in the Stomach" as Required by the Asserted Claims of the '927, '756 and '989 Patents.

281. Claims 18, 25, 26, 34, 61 and 62 of the '927 Patent, claims 1, 2, 5, 6, 7 and 11 of the '756 Patent and claim 10 of the '989 Patent require that the tablet, when administered, "swells . . . to increase its size to promote gastric retention of the dosage form in the stomach." (5/14/2014 Tr. 519:13-520:25.)

282. Depomed relies on swelling studies conducted by a laboratory it retained, EAG, and Actavis' swelling study conducted at FDA's request. (5/12/2014 Tr. 162:13-16; 5/13/2014 Tr. 279:16-19.) [redacted] The methods involve either shaking or swirling the tablet in simulated gastric fluid. These conditions are chosen to minimize the deformation of the tablets during testing. (5/12/2014 Tr. 130:10-131:10.)

283. Dr. Annunziata explained, however, that the stomach breaks down larger food particles into smaller food particles through serial retropulsion and other destructive forces. (5/12/2014 Tr. 153:20-25; 5/13/2014 Tr. 237:7-13.) The scientific literature criticizes static models as not accurately reflecting the conditions found in a fed stomach. (5/13/2014

Tr. 237:19-238:7, 240:12-15) The scientific literature instead recommends using commercially available "dynamic" models, as they account for more of the destructive forces found in the stomach in the fed mode. [redacted]

Dr. Hopfenberg testified that he did no study as to whether the presence of food in the fed mode would have any impact on the swelling behavior of the Actavis tablet. (5/12/2014 Tr. 487:5-8.)

284. Furthermore, Depomed's experts failed to draw a link between the results of the *in vitro* swelling studies and any swelling that might occur in the stomach. (5/13/2014 Tr. 239:4-11, 280:8-18.) For example, Depomed's own expert Dr. Annunziata testified that he could not say as a matter of reasonable scientific certainty whether Actavis' ANDA Tablets swell in the stomach when subjected to all of the mechanical forces in the stomach to the same extent they would swell in the *in vitro* studies performed by Depomed and Actavis. (5/13/2014 Tr. 239:4-11.) Additionally, Dr. Williams did not consider whether one could extrapolate the *in vitro* swelling data to *in vivo* data with food in the stomach, nor did he conduct any investigation as to whether the dimensions of the tablets would be the same in a stomach as in a static model. (5/13/2014 Tr. 280:8-18, 299:3-21.) In fact, Drs. Felton and Derendorf repeatedly insisted that *in vitro* data does not replicate *in vivo* conditions. (5/19/2014 Tr. 974:4-12, 995:22-25, 996:8-21, 997:11-12, 998:2-4, 998:14-22, 1023:13-20, 1029:6-7.)

285. Instead, the more reasonable inference is that Actavis' tablets will not swell to the same extent in a stomach in the fed mode as the *in vitro* data in the Actavis and EAG swelling studies would suggest. As Dr. Friend and Dr. Annunziata explained, the destructive forces in the stomach would act on the tablet just as much as they would on food particles. (5/12/2014 Tr. 157:4-13; 5/14/2014 Tr. 522:1-8.) Static swelling studies, therefore, have "little to no

relevance" standing alone as to whether and to what extent the tablet would swell in the stomach in the fed mode. (5/14/2014 Tr. 522:1-8.)

286. That Actavis' ANDA products are gastric retained does not mean that the tablets swell in the stomach, much less to a particular size. (5/13/2014 Tr. 235:9-19; 5/14/2014 Tr. 525:14-17.) Dr. Annunziata explained that any particles over two to three millimeters in size can be gastric retained for a significant period of time. (5/12/2014 Tr. 155:10-16.) Actavis' ANDA Products exceed this size without any swelling. (5/13/2014 Tr. 252:15-18, 252:22-253:1.) Dr. Annunziata also explained that tablets and other materials can be gastric retained even in the absence of swelling. (5/13/2014 Tr. 252:22-253:1, 254:2-4.) He explained that a special camera-containing non-swelling capsules that are about 23 mm by 11 mm in diameter can be gastric retained for "an hour or two hours, three hours, sometimes even longer than that." (5/13/2014 Tr. 220:19-21.)

287. Furthermore, in the EAG swelling studies, the technician performing the experiments noted that, during testing, Actavis' ANDA Products began floating in the simulated gastric fluid. (5/12/2014 Tr. 129:22-25; PTX 332 at DEPOACT0975179.1.) Floating of the dosage form in the stomach would be an alternative way in which gastric retention is promoted, that is independent of and unrelated to any swelling of Actavis' ANDA Products that may occur.

288. Furthermore, Dr. Annunziata explained that, when Actavis' ANDA Products are exposed to simulated gastric fluid, they get soft and sticky. (5/13/2014 Tr. 238:8-10.) He further explained that such sticky materials can adhere to the sides of the stomach and become gastric retained for that reason. (Id. at 225:16-21.) Again, gastric retention because of adherence would be independent of and unrelated to any swelling of Actavis' ANDA Products that may occur.

289. Depomed has not put forward any evidence regarding the doctrine of equivalents. Moreover, allowing Depomed to argue that a pharmaceutical composition meets this limitation without substantial evidence of swelling in the stomach would render this limitation meaningless, thereby improperly vitiating the limitation.

290. Thus, for these reasons, gastric retention is not a reliable indication that Actavis' ANDA Products swell in the stomach.

291. Depomed has therefore failed to establish Actavis' ANDA Products will "***swell*** . . . to promote gastric retention of the dosage form ***in the stomach of the mammal***" as required by all of the asserted claims of the '927, '756 and '989 Patents. (5/14/2014 Tr. 521:5-6.)

2. Actavis' ANDA Products Do Not Contributorily Infringe or Induce Infringement of the Method of Treatment Claims in the '927, '756, '332 and '992 Patents.

292. Claims 18, 25, 26, 34, 61 and 62 of the '927 Patent, claims 6, 7 and 11 of the '756 Patent, claims 17 and 24 of the '332 Patent and claim 22 of the '992 Patent are directed to methods of treatment involving administration of a gastric retained dosage form comprising gabapentin (collectively, the "Method Claims").

293. Because Actavis does not directly administer its ANDA products to patients, Depomed does not contend that these claims are directly infringed. (D.I. 328, Supplement to Ex. 1.) Instead, Depomed only alleges that indirect infringement of these claims – that is, that Actavis contributorily infringes or induces the infringement of these claims. (Id.)

294. With respect to the asserted claims of the '927 and '756 Patents, as described above, Depomed has failed to prove that Actavis' ANDA Products "swells . . . to increase its size to promote gastric retention of the dosage form in the stomach of the mammal," as required by the claims. In the absence of direct infringement of the claims of the '927 and '756 Patents, there can be no indirect infringement.

295. Depomed also has adduced no evidence from Actavis' current or former employees regarding any specific intent to infringe any of the asserted patents.

296. Furthermore, Depomed has failed to demonstrate that Actavis intends to induce others to infringe or contributorily infringe the Method Claims. [redacted] Although Dr. Brown testified that the categories of off-label uses can "contain" neuropathic pain, that leaves open the probability that there are also non-neuropathic off-label uses for Gralise. That Dr. Brown is unaware of uses of Gralise other than for the treatment of pain is unsurprising as her clinical specialty is in the management of pain. (5/16/2014 Tr. 866:24-25.)

297. Dr. Williams testified that doctors are free to prescribe Gralise for both approved and off-label uses and that off-label uses are not approved by FDA. (5/13/2014 Tr. 304:20-305:1.)

298. In view of the existence of a large off-label market for gabapentin products, including Gralise, Depomed has failed to demonstrate that there are no substantial noninfringing uses for Actavis' ANDA Products.

B. Actavis' 600 mg ANDA Product Does Not Infringe The '962 Patent Because It Is Not An Oval.

299. Claim 1 of the '962 Patent requires that the dosage form have "a shape which when projected onto a plane, is either an oval[7] or a parallelogram." (JTX 1 at col. 11, ll.24-26; Stip. Fact ¶ 43.) Claims 5, 8, and 10 are dependent upon claim 1 and claim 13 is dependent upon

[7] Depomed does not contend that Actavis' 600 mg gabapentin once-daily tablet is in the shape of a parallelogram. Thus, the "oval" shape is the only issue in this case.

claim 10. (JTX 1; Stip. Fact ¶ 42.) Thus, claims 5, 8, 10 and 13 of the '962 Patent require that the dosage form has "a shape which when projected onto a plane, is either an oval or a parallelogram."

300. Depomed admits that Actavis' 300 mg ANDA Product does not infringe the '962 Patent. (See Stip. Fact ¶ 41.) Thus, the only product accused of infringing the '962 Patent is Actavis' 600 mg ANDA Product.

301. The '962 Patent states that:

> Some of the possible shapes are oval, triangle, almond, peanut, 'bow tie,' parallelogram, trapezoidal, pentagonal, and hexagonal, provided (as stated above) that the largest planar projection of the shape has at least two orthogonal dimensions, one being larger than the other. Preferred shapes are oval and parallelogram (notably diamond-shaped, i.e., a quadrilateral in which opposing sides are parallel and adjacent sides are not at right angles). . . . Particularly preferred shapes are those that have three (orthogonal) planes of symmetry to aid in swallowing.

(JTX 1 at col. 4, ll. 10-21.) Dr. Hopfenberg explained that these shapes disclosed in the specification of the '962 Patent are recognized in the art to be distinct shapes. (5/14/2014 Tr. 467:3-17, 469:6-7, 468:17-19.) The '962 Patent also criticizes "tablet or caplets (cylindrical tablets with rounded ends) that are elongated in shape to facilitate swallowing." (JTX 1 at col. 3, ll. 1-19.) The '962 Patent explains that these shapes may orient in the vicinity of the pylorus such that their longest dimension is in alignment with the pyloric axis, and therefore pass through the pylorus without being gastric retained. (Id.)

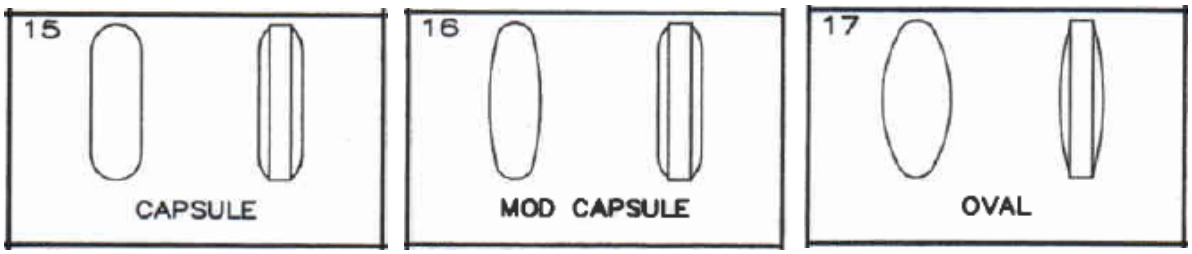
302. Depomed has not put forward any evidence regarding the doctrine of equivalents. Depomed amended the claims to limit the shapes of the tablet to an "oval or parallelogram" during prosecution of the '962 Patent to overcome the PTO Examiner's rejection of the pending claims in view of the prior art. (JTX 9 at DEPOACT0002365; 5/14/2014 Tr. 469:24-470:8.) Thus, Depomed disclaimed and dedicated to the public other shapes, such as triangle, almond,

peanut, "bow tie," trapezoidal, pentagonal, and hexagonal, as well as elongated tablet and caplet shapes. (See JTX 1 at col. 3, ll. 1-19, col. 4, ll. 7-17.) Depomed's disclaimer of these other shapes also makes clear that the term "oval" should be applied narrowly so as to not encompass shapes that Depomed distinguished and disclaimed, such as elongated tablet and caplet shapes, almond shapes and the like.

303. Actavis' ANDA consistently states that the 600 mg product is "capsule shaped," including on its label, also as testified to by Dr. Hejazi. (5/12/2014 Tr. 83:17-20, 84:3-6, 84:9-11, 84:21-24, 85:22-24, 86:3-87:5; 5/14/2014 Tr. 515:21-23; PTX 14 at ACTGAB000000352-353, 357, 366; DTX 23 at ACTGAB000321392; DTX 31 at ACTGAB000321127; DTX 36 at ACTGAB000000745.) There is only one isolated deviation from this where Actavis used the word "oval" once in a purchase requisition. (5/12/2014 Tr. 87:24-88:1; PTX 44.) In its ANDA, however, Actavis consistently and repeatedly characterized its 600 mg Product as being "capsule shaped" in contrast to the "oval shaped" Gralise tablets. (5/12/2014 Tr. 83:17-20, 84:3-6, 84:9-11, 84:21-24, 85:22-24, 86:3-87:5; 5/14/2014 Tr. 515:21-23; PTX 14 at ACTGAB000000352-353, 357, 366; DTX 23 at ACTGAB000321392; DTX 31 at ACTGAB000321127; DTX 36 at ACTGAB000000745.) The single, isolated use of the word "oval" by Actavis (5/12/2014 Tr. 87:24-88:1; PTX 44) does not constitute an admission concerning the shape of Actavis' 600 mg ANDA Product.

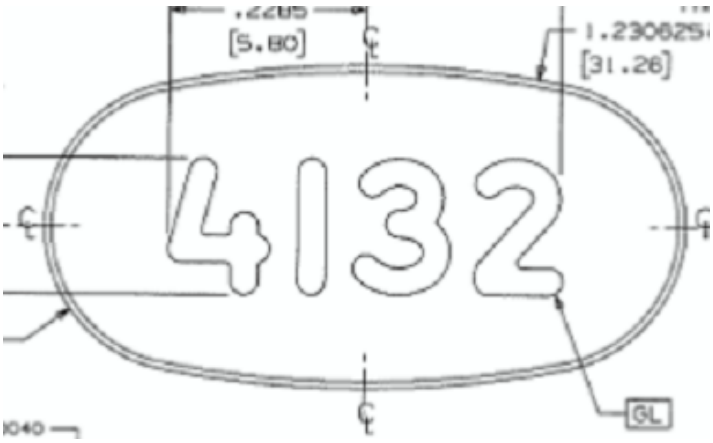
304. There are a limited number of shapes that are commonly used in manufacturing pharmaceutical tablets. Dr. Friend points to a TABLETING SPECIFICATION MANUAL that describes about 25 such shapes. (5/14/2014 Tr. 508:8-25; DTX 39.) Dr. Hopfenberg testified regarding a TABLET DESIGN TRAINING MANUAL from the Elizabeth Carbide Die Company that contains a table showing similar tablet shapes. (5/14/2014 Tr. 472:15-473:11, 477:9-22.)

305. The American Pharmacists Association, in their TABLETING SPECIFICATION MANUAL, clearly differentiates an oval from a modified capsule, which is the shape of Actavis' 600 mg tablet. (5/14/2014 Tr. 511:8-18; DTX 39 at Fig. 15-17.)



(DTX 39 at Fig. 15-17.) Dr. Friend explained that these are distinct shapes in the pharmaceutical arts. (5/14/2014 Tr. 512:7-14.) He explained that "the primary difference between the capsule and modified capsule is the slight widening towards the center of the tablet." (5/14/2014 Tr. 511:19-512:4.) In contrast, the oval is a continuous curve along the side as opposed to the disjointed curves that create the slight widening seen on the side of the modified capsule. (Id. at 512:5-512:21.) Dr. Hopfenberg similarly testified, based on the ENCYCLOPEDIA OF PHARMACEUTICAL TECHNOLOGY, that oval tablet shapes are distinct from capsule and modified capsule tablet shapes (as well as other shapes like almond shapes, peanuts, and bow tie shapes). (Id. at 477:9-22.)

306. The curvature of Actavis' 600 mg ANDA Product is not as pronounced as the oval shapes depicted in the TABLETING SPECIFICATION MANUAL or the ENCYCLOPEDIA OF PHARMACEUTICAL TECHNOLOGY relied upon by the experts in this case. (5/14/2014 Tr. 472:15-473:11, 477:9-22, 511:8-512:4, 512:5-512:21; DTX 39 at Fig. 17.) For example, the drawing for the punches used to make the tablets show the following profile for the tablets:



(PTX 57.) [redacted]

[redacted]

[redacted] The long sides of the tablet appear substantially parallel, with only a slight outward curvature. (See 5/14/2014 Tr. 511:19-512:4; DTX 39 at Fig. 15 and 16.) This shape is thus consistent with either the capsule or modified capsule tablet shape described in the TABLETING SPECIFICATION MANUAL and the ENCYCLOPEDIA OF PHARMACEUTICAL TECHNOLOGY references. (DTX 39 at Fig. 25; 5/14/2014 Tr. 472:15-473:11, 477:9-22.) Because the sides of the tablet are not substantially curved as an oval tablet depicted in the Tableting Publications (DTX 39 at Fig. 17; 5/14/2014 Tr. 472:15-473:11, 477:9-22, 512:5-512:21), it is not an oval shape as understood in the art.

307. Thus, Actavis' 600 mg ANDA Product does not meet the claim limitation "a shape which when projected onto a plane, is either an oval or a parallelogram," and thus does not infringe the asserted claims of the '962 Patent. (5/14/2014 Tr. 517:2-12.)

308. Depomed did not present any evidence that the asserted claims of the '962 patent are infringed under the doctrine of equivalents. In any event, because the "oval" limitation was added by amendment during prosecution of the '962 Patent, prosecution history estoppel bars Depomed from raising the doctrine of equivalents with respect to this limitation.

C. Actavis' ANDA Products Do Not Infringe the '280 Patent (the Platform Patent) Because, When Swollen, They Are Not a Size Exceeding the Pyloric Diameter in the Fed Mode.

309. Claim 1 of the '280 Patent requires that the dosage form swell to "a size exceeding the pyloric diameter in the fed mode to promote retention in the stomach during said fed mode." (JTX 2 at col. 17, ll. 53-55; Stip. Fact ¶ 53.) Claims 12, 14, and 45 are dependent upon claim 1. (JTX 2; Stip. Fact ¶ 52.) Thus, claims 1, 12, 14, and 45 of the '280 Patent require that the dosage form swells to "a size exceeding the pyloric diameter in the fed mode to promote retention in the stomach during said fed mode." As explained above, any dosage form, including Actavis' ANDA Products, would far exceed the dimensions of a clenched pylorus. (5/13/2014 Tr. 252:15-18, 254:2-4.) Thus, the pyloric diameter here refers to the diameter of the pylorus during the brief periods of relaxation when larger materials can escape the stomach, and not the periods of time during which the pylorus is clenched tightly closed to prevent the stomach contents from being expelled into the intestines.

310. As an initial matter, Dr. Annunziata admitted that particles that are smaller than the diameter of the relaxed pylorus in the fed mode can still be retained in the stomach during the fed mode. (5/13/2014 Tr. 235:9-19.) Thus, evidence of gastric retention is not probative of the size of Actavis' ANDA Products when in the fed stomach. (Id. at 235:9-19.)

311. As explained above, Depomed has failed to demonstrate that Actavis' ANDA Products swell in the stomach in the fed mode, much less to a particular size exceeding the pyloric diameter. (See *supra*, ¶¶ 282-289.) But even if Depomed's evidence of swelling is

accepted, Depomed has failed to demonstrate that the swollen dimensions of Actavis' ANDA Products exceed the size of the pyloric diameter in the fed mode.

312. [redacted]

313. As Dr. Annunziata admitted, the pyloric diameter is "definitely variable as everybody, every person is variable, in size, shape, et cetera" and so he could not say with reasonable scientific certainty whether 12 millimeters or even 20 millimeters exceeds the size of the pyloric diameter. (5/13/2014 Tr. 244:12-15; 245:25-246:22, 249:16-21, 249:22-250:13, 252:19-22.)

314. Dr. Friend explained that the fed mode concludes after 180 minutes for most people – a figure that was not disputed by Dr. Annunziata. (5/14/2014 Tr. 532:11-15, 531:13-23, 532:16-533:2; 5/13/2014 Tr. 232:1-233:2.)

315. For Actavis' 300 mg ANDA Product, up to 180 minutes, the tablet always remains 20 millimeters or smaller in every dimension (length, width and height). (5/14/2014 Tr. 532:11-15, 531:13-23, 532:16-533:2.) Depomed's experts were unable to state with

reasonable scientific certainty that these dimensions exceed the size of the pylorus in the fed mode. (5/13/2014 Tr. 249:16-21.)

316. As explained above, the most precise data available from scientific publications suggests that the pyloric diameter is 12.8 mm ± 7.0 mm, or a range of 5.8 mm to 19.8 mm. (5/13/2014 Tr. 242:24-243:4, 244:16-246:18; 5/14/2014 Tr. 527:11-528:9; PTX 245 at DEPOACT0114761.) For Actavis' 300 mg ANDA Product, up to 180 minutes, the width and height dimensions never exceed this range but instead falls squarely within it. (5/14/2014 Tr. 532:11-15, 531:13-23, 532:16-533:2.) With respect to the length of Actavis' 300 mg ANDA product, only at 180 minutes, when the fed mode is expiring, does the product reach 20 mm in length. (Id. at 531:24-532:10, 510:25-511:3.)

317. These dimensions are likely an overestimate of the actual size to which the tablets will swell when in the fed stomach. (5/13/2014 Tr. 237:7-238:7.) The experts agree that the tablets in a fed stomach will be subjected to destructive forces. (5/13/2014 Tr. 237:7-13.) These will tend to reduce the amount of swelling of the tablet compared to the gentle *in vitro* conditions which were chosen to avoid deforming the tablet. (5/12/2014 Tr. 130:10-131:10.) Because Actavis' 300 mg ANDA Product does not swell to a size exceeding the pyloric diameter in the fed mode under even the gentle *in vitro* testing conditions (see PTX135), it is even less likely to do so when in a fed stomach. Accordingly, Depomed has failed to demonstrate that Actavis' 300 mg ANDA product, when swollen, exceeds the size of the pyloric diameter in the fed mode.

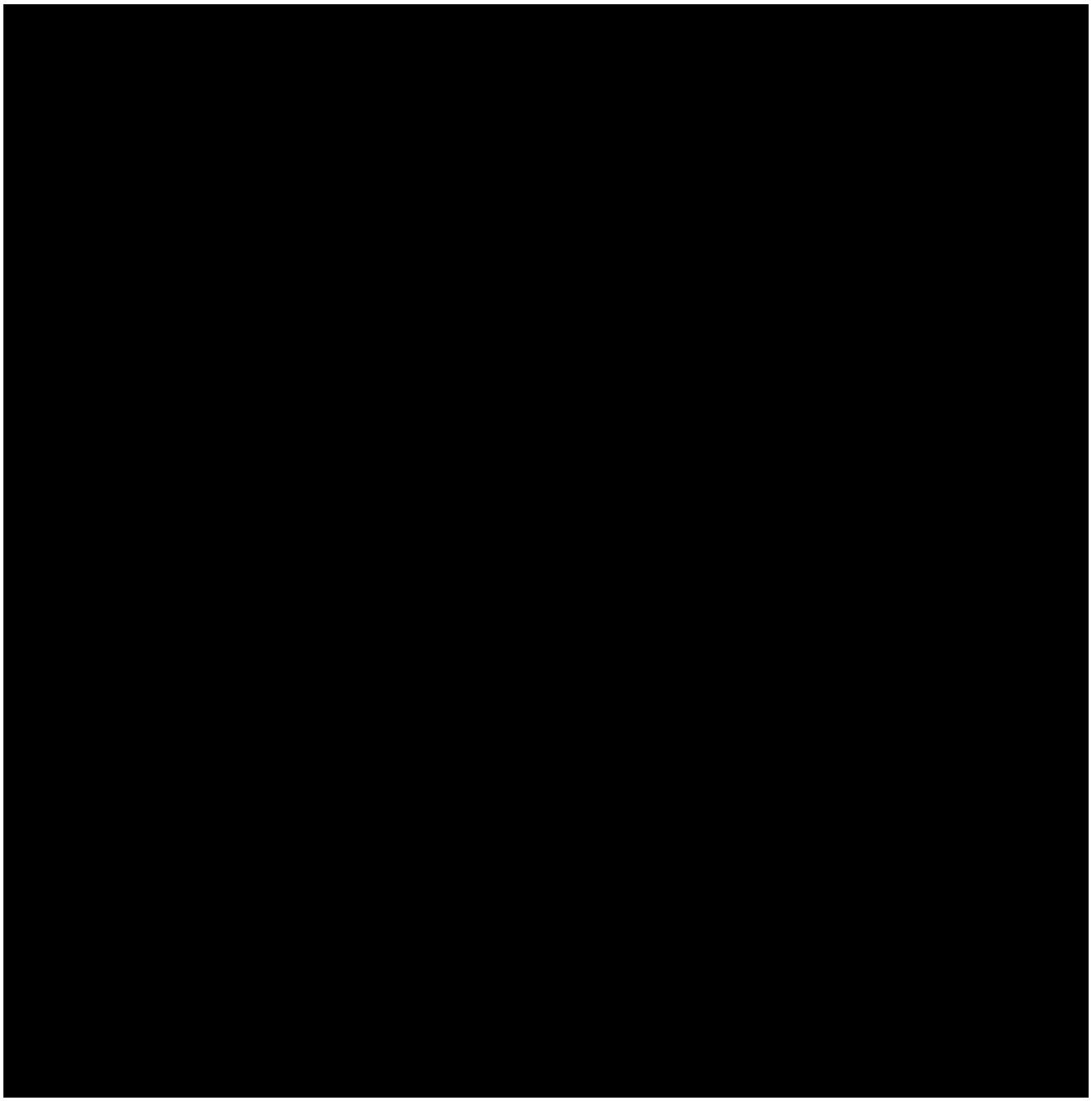
318. With respect to Actavis' 600 mg ANDA Tablet, the width and height dimensions of the tablets are always smaller than 20 mm. (5/14/2014 Tr. 532:11-15, 531:13-23, 532:16-533:2.) Accordingly, as explained above, these dimensions cannot be said to exceed the size of the pyloric diameter in the fed mode.

319. [redacted] Dr. Annunziata was unable to state as a matter of reasonable scientific certainty that these dimensions exceed the pyloric diameter in the fed mode. (5/13/2014 Tr. 239:4-11, 249:16-250:13.)

320. When compared to the most precise measurements of the pyloric diameter reported in the scientific literature (i.e., 12.8 mm ± 7.0 mm, or a range of 5.8 mm to 19.8 mm), however, Actavis' 600 mg ANDA Product is a size exceeding the pyloric diameter (i.e., 20 mm) in its dry state before swelling, and only grows larger from there. (5/14/2014 Tr. 534:1-4.) This means that the swelling is not responsible for the length dimension being larger than the pyloric diameter as required by the '280 Patent claims.

321. For these reasons, Depomed has failed to meet its burden of demonstrating that Actavis' 600 mg ANDA Product, when swollen, is of a size exceeding the pyloric diameter in the fed mode.

322. [redacted]



323. Depomed has not put forward any evidence regarding the doctrine of equivalents.

Depomed is barred by prosecution history estoppel from asserting the doctrine of equivalents

because the limitation "a size exceeding the pyloric diameter in the fed mode" was added by amendment for purposes of patentability. (See, *supra*, ¶ 23.)

324. Thus, these data also do not demonstrate that Actavis' ANDA Products infringe the asserted claims of the '280 Patent. (5/14/2014 Tr. 534:11-15.)

CONCLUSIONS OF LAW

325. Subject matter jurisdiction over this matter is proper pursuant to 28 U.S.C. §§ 1331, 1338, and 2201. Venue is proper in this court under 28 U.S.C. §§ 1391 and 1400(b). For the reasons set forth below: (1) all asserted claims of the '927, '989, '756, '332, '992 and '962 Patents are invalid due to obviousness; (2) all asserted claims of the '280 Patent are invalid due to indefiniteness; and (3) the Actavis ANDA Products will not directly or indirectly infringe claims 1, 12, 14 and 45 of the '280 Patent, claims 5, 8, 10 and 13 of the '962 Patent, claims 18, 25, 26, 34, 61 and 62 of the '927 Patent, claim 10 of the '989 Patent, claims 1, 2, 5, 6, 7 and 11 of the '756 Patent, claims 17 and 24 of the '332 Patent or claim 22 of the '992 Patent.

I. THE '927, '989, '756, '332 AND '992 PATENTS ARE INVALID FOR OBVIOUSNESS

A. Obviousness is Established by Showing that a Person of Ordinary Skill in the Art Could Combine Known Elements with a Reasonable Expectation of Success.

326. Section 103(a) provides that a patent may not be obtained "if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious to a person having ordinary skill in the art." 35 U.S.C. § 103(a). Obviousness is a question of law that is predicated on several factual inquiries. See Richardson-Vicks v. Upjohn Co., 122 F.3d 1476, 1479 (Fed. Cir. 1997). Specifically, obviousness is determined in view of four considerations: (1) the scope and content of the prior art; (2) the level of ordinary skill in the art; (3) the differences between the claimed subject matter and the prior art; and (4) secondary considerations of non-obviousness, such as commercial success, long felt but unsolved need, failure of others, acquiescence of others in the industry that the patent is valid, and unexpected results. See Graham v. John Deere Co., 383 U.S. 1, 17-18 (1966).

327. A party seeking to challenge the validity of a patent based on obviousness must demonstrate by "clear and convincing evidence" that the invention described in the patent would have been obvious to a person of ordinary skill in the art at the time the invention was made. Allergan, Inc. v. Sandoz Inc., 726 F.3d 1286, 1291 (Fed. Cir. 2013), cert. denied, 134 S. Ct. 1764 (2014). In determining what would have been obvious to one of ordinary skill in the art, the use of hindsight is not permitted. See KSR Intern. Co. v. Telejlex, Inc., 550 U.S. 398, 421 (2007) (cautioning the trier of fact against "the distortion caused by hindsight bias"). In KSR, the Supreme Court also rejected the rigid application of the principle that there should be an explicit "teaching, suggestion, or motivation" in the prior art, the nature of the problem, or the knowledge of a person having ordinary skill in the art, in order to find obviousness. See KSR, 550 U.S. at 415. The KSR Court acknowledged though the importance of identifying "'a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does' in an obviousness determination." Takeda Chem. Indus. v. Alphapharm Pty. Ltd., 492 F.3d 1350, 1356-57 (Fed. Cir. 2007) (quoting KSR, 550 U.S. at 418).

328. "Obviousness does not require absolute predictability of success," but rather, requires "a reasonable expectation of success." See Medichem, S.A. v. Rolado, S.L., 437 F.3d 1157, 1165 (Fed. Cir. 2006) (quoting In re O'Farrell, 853 F.2d 894, 903-04 (Fed. Cir. 1988)). To this end, obviousness "cannot be avoided simply by a showing of some degree of unpredictability in the art so long as there was a reasonable probability of success." Pfizer, Inc. v. Apotex, Inc., 480 F.3d 1348, 1364 (Fed. Cir. 2007). Moreover, while the Federal Circuit has noted that pharmaceuticals can be an "unpredictable art" to the extent that results may be unexpected, it also recognizes that, per KSR, evidence of a "finite number of identified,

predictable solutions" or alternatives can support a finding of obviousness. See Hoffmann-La Roche Inc. v. Apotex Inc., No. 2013-1164, 2014 WL 1394948 (Fed. Cir. Apr. 11, 2014).

329. In sum, a claimed combination of prior art elements is obvious if the elements were known or within the technical grasp of the skilled artisan and he or she would reasonably expect the combination of elements to work. KSR, 550 U.S. at 421; PharmaStem Therapeutics, Inc. v. ViaCell, Inc., 491 F.3d 1342, 1360 (Fed. Cir. 2007) (reversing the jury verdict to find the patent obvious).

B. The Person of Ordinary Skill in the Art

330. Obviousness is determined from the perspective of a person of ordinary skill in the art at the time the invention was made. See In re O'Farrell, 853 F.2d at 902. A person of ordinary skill in the art may be defined according to several factors, including: "(1) the inventor's educational background; (2) the kinds of problems confronted in the art; (3) solutions found previously; (4) the level of sophistication of the technology; (5) the speed of innovation in the art; and (6) the educational level of active workers in the field." Daiichi Pharm. Co., Ltd. v. Apotex, Inc., 380 F. Supp. 2d 478, 484 (D.N.J. 2005) (citation omitted).

331. The parties proposed definitions of a person of ordinary skill in the art are not materially different as both parties' experts agree that the other party's definition would not alter their opinions. (FOF ¶ 138.)

332. A person of ordinary skill in the art as a person with a Ph.D. in chemistry, chemical engineering, pharmaceutical sciences or a related discipline. Alternatively, the person could have a master's degree in one of those fields with at least two years of practical experience and alternatively, the person could have a bachelor's degree in one of those fields with even more practical experience. (FOF ¶ 137.)

C. The Asserted Claims of the Gabapentin Patents Would Have Been Obvious

1. The Asserted Claims of the '927 Patent Would Have Been Obvious in View of Depomed's WO '107 and Rowbotham.

333. Depomed asserted claims 18, 25, 26, 34, 61 and 62 of the '927 Patent. (FOF ¶ 26.) Each of the asserted claims depend from either of two independent claims – claim 17 or claim 33 – neither of which is asserted in this litigation. (FOF ¶ 39.)

334. The claims 18, 25, 26, 34, 61 and 62 of the '927 Patent would have been obvious to one of ordinary skill over Depomed's WO '107 (DTX 234) in view of Rowbotham (DTX 313), along with the knowledge of a person of ordinary skill in the art as evidenced McLean (DTX 267) and Stevenson (PTX 500).

a) Depomed's WO '107 and Rowbotham Disclose All of the Limitations of Claims 17 and 33 of the '927 Patent.

335. All the elements of claims 17 and 33 of the '927 Patent were known or within the technical grasp of the skilled artisan. (FOF ¶¶ 141-149.)

336. Claim 17 of the '927 Patent is directed to a "method of treating neuropathic pain in a mammal comprising administering a therapeutically effective amount of a daily dosage of about 100 mg to about 4800 mg of gabapentin or a pharmaceutically acceptable salt thereof." (FOF ¶ 40.) Claim 33 of the '927 Patent is directed to a "method of administering a therapeutically effective amount of a daily dosage of about 100 mg to about 4800 mg of gabapentin to a mammal." (FOF ¶ 41.) Rowbotham discloses daily doses of 300 mg up to 3600 mg gabapentin per day were effective to treat pain and sleep interference associated with post-herpetic neuralgia, a type of neuropathic pain. (FOF ¶ 143.)

337. Claims 17 and 33 of the '927 Patent require the gabapentin to be "dispersed in a gastric retained dosage form to the mammal in which a fed mode has been induced." (FOF

¶¶ 40-41.) Depomed's WO '107 discloses an orally administered, gastric retained, controlled release formulation for use with a highly soluble drug when "administered to a subject who is in the digestive or 'fed' mode." (FOF ¶ 144.)

338. Claims 17 and 33 of the '927 Patent require "the dosage form comprises a single polymer matrix comprising at least one swellable hydrophilic polymer that swells in a dimensionally unrestrained manner by imbibing water to increase its size to promote gastric retention of the dosage form in the stomach of the mammal." (FOF ¶¶ 40-41.) Depomed's WO '107 discloses that the "drug is dispersed in a polymeric matrix, and that matrix is water swellable." (FOF ¶ 145.) WO '107 further discloses that the "matrix is a relatively high molecular weight polymer that swells upon ingestion to achieve a size that is at least about twice its unswelled volume and that promotes gastric retention during the fed mode." (Id.) WO '107 discloses that the "water swellable polymer forming the matrix . . . is any polymer . . . that swells in a dimensionally unrestricted manner upon imbibition of water, and that provides for sustained release of an incorporated drug." (FOF ¶ 145.)

339. Claims 17 and 33 of the '927 Patent require " upon contact with water, gabapentin is released by diffusion from the dosage form over a period of at least five hours and at least 40 wt% of the gabapentin is retained in the dosage form one hour after administration." (FOF ¶¶ 40-41.) Depomed's WO '107 discloses that drug is released for at least five hours from the dosage forms. (FOF ¶ 147.) WO '107 discloses that the "amount of polymer [in the dosage form] will be sufficient . . . to retain at least about 40% of the drug within the matrix one hour after ingestion (or immersion in the gastric fluid)." (FOF ¶ 148.)

340. Actavis has therefore established by clear and convincing evidence that all the elements of claims 17 and 33 of the '927 Patent were known or within the technical grasp of the skilled artisan. KSR, 550 U.S. at 421; PharmaStem Therapeutics, 491 F.3d at 1360.

b) **One of Ordinary Skill in the Art Would Have Been Motivated to Combine Depomed's WO '107 and Rowbotham.**

341. As the Supreme Court has made clear: "if a technique has been used to improve one device, and a person of ordinary skill in the art would recognize that it would improve similar devices in the same way, using the technique is obvious unless its actual application is beyond his or her skill." KSR, 550 U.S. at 417. Generally, "[c]ontrolled release delivery systems are known to offer advantages over conventional dosage forms, including increased patient compliance with prescriptions, decreased total drug delivery, and decreased side effects." Purdue Pharma Products L.P. v. Par Pharm., Inc. ("Purdue I"), 642 F. Supp. 2d 329, 336 (D. Del. 2009) dismissed, 370 F. App'x 80 (Fed. Cir. 2009) and aff'd, 377 Fed. App'x 978, 336 (Fed. Cir. 2010) ("Purdue II") (affirming district court decision of obviousness of controlled release formulation of prior art drug); see also Alza Corp. v. Mylan Labs., Inc. ("Alza II"), 464 F.3d 1286 (Fed. Cir. 2006) (same), aff'g, ("Alza I") 388 F. Supp. 2d 717 (N.D. W. Va. 2005).

342. Although Depomed's WO '107 does not explicitly mention gabapentin, one of ordinary skill in the art would have been motivated to formulate gabapentin in the WO '107 gastric retained dosage form to alleviate the burden on patients to take multiple doses per day, improve patient compliance, and reduce the incidence of side effects. (FOF ¶¶ 150-151.)

343. One of ordinary skill in the art would have known that gabapentin was not suitable for a conventional controlled-release dosage form and that the only viable approach to making a controlled-release form of gabapentin would be to use a gastric retentive system in order to hold the gabapentin in a place above its window of absorption for an extended period of

time. (FOF ¶ 152.) Named inventor, Dr. Hou, confirmed that it was gabapentin's known absorption characteristics that made it such a good candidate for a gastric retained controlled-release dosage form. (FOF ¶ 153.)

344. One of ordinary skill in the art would have been motivated to use the dosage form disclosed in Depomed's WO '107 because those formulations were ideal for drugs of high solubility where the drug needed to be "absorbed mostly in the stomach or high in the gastrointestinal tract." (FOF ¶ 155.) One of ordinary skill in the art would have been further motivated to replace the metformin as disclosed in WO '107 with gabapentin because both drugs were known to exhibit saturable absorption high in the gastrointestinal tract. (Id.) This is because a controlled-release gastric retained dosage form would improve issues relating to saturation. (Id.)

345. Although Depomed argues that there was no motivation to put gabapentin in Depomed's WO '107 dosage form (FOF ¶ 156), the argument is not persuasive. Although gabapentin is not explicitly mentioned in WO '107, the disclosed dosage form is described as being useful for a number of drugs that are all soluble and have a window of absorption high in the gastrointestinal tract; therefore, one of ordinary skill in the art would understand the WO '107 is not limited to metformin or the drugs specifically identified in WO '107. (FOF ¶ 157.) Although metformin is chemically different from gabapentin, these differences are outweighed by their similarities. (FOF ¶ 158.) Although Depomed's experts suggest gabapentin's propensity to slowly degrade in certain environments would teach away from a gastric retained dosage form, they ignore that the prior art provides a solution for these issues – that hydrophilic polymer matrices trap the drug in the internal, dry core, protecting the drug from the stomach's acid until it is dissolved and released by penetrating gastric fluid. (FOF ¶ 159.)

346. Depomed's experts also testified as to the inter-person variability in the absorption of gabapentin; however, came forward with no evidence that this variability had any impact on gabapentin's clinical efficacy. (FOF ¶ 160.) Depomed's experts further argue that there was no known relationship between gabapentin's pharmacokinetics and its pharmacodynamics; however, Depomed's experts admit the decade of experience with immediate release gabapentin would provide a target that formulators would seek to obtain using a controlled-release formulation and that the lack of a pharmacokinetic – pharmacodynamic relationship for gabapentin did not prevent Pfizer and various generics from bringing gabapentin products to the U.S. market. (FOF ¶ 161.) Lastly, Depomed's experts argue that a food effect would have cast doubt on an expectation of success, yet the literature states that food has no clinically significant effect on gabapentin and all of Depomed's experts admit that the food effect was not clinically significant. (FOF ¶ 162.)

347. Lastly, although Depomed also argues that WO '812 teaches away from a matrix dosage form being gastric retained (FOF ¶ 163), this argument is without merit as WO '812 does not criticize swellable gastric-retained dosage forms nor does WO '812 focus on highly soluble drugs. (Id.) For a reference to teach away, there must be more than an expression of a "general preference for an alternative invention," it must "criticize, discredit, or otherwise discourage investigation into the invention claimed." Galderma Labs., L.P. v. Tolmar, Inc., 737 F.3d 731, 738 (Fed. Cir. 2013) cert. denied, No. 13-1350, 2014 WL 1882766 (U.S. June 9, 2014) (citing Depuy Spine, Inc. v. Medtronic Sofamor Danek, Inc., 567 F.3d 1314, 1327 (Fed. Cir. 2009)). The Federal Circuit further explained that "[a] teaching that a composition may be optimal or standard does not criticize, discredit, or otherwise discourage investigation into other compositions." Id. at 739. A preference for an alternate embodiment does not equate to

criticizing, discrediting or discouraging investigation of another embodiment. Hoffman-La Roche Inc. v. Apotex Inc., 2012 WL 1637736, at *11 (D.N.J. May 7, 2012). WO '812 cannot be said to teach away because it merely provides an alternative way of causing a dosage form to be gastric retained. In any event, WO '812 is not directed to highly water soluble drugs the same way that WO '107 and WO '128 are and thus one of ordinary skill in the art would have focused instead on the more relevant prior art in combining the teachings of the prior art. (See DTX 229 (making no mention of highly water soluble drugs).)

348. Actavis has therefore established by clear and convincing evidence that a person of ordinary skill in the art would recognize that the controlled release, gastric retained formulations disclosed in Depomed's WO '107 would improve gabapentin absorption and pharmacokinetics in the same way those formulations improved other highly water soluble drugs such as metformin, captopril and ranitidine. (FOF ¶¶ 150-163.) Metformin and gabapentin share properties relevant to their absorption by the human body after ingestion – namely, high water solubility, a narrow window of absorption in the upper GI tract and absorption via a saturable transporter. (FOF ¶ 155.) Therefore, gabapentin, just like metformin, would have been well suited to a gastric retained, controlled release formulation. (FOF ¶ 152.)

c) **One of Ordinary Skill in the Art Would Have Had a Reasonable Expectation of Success in Combining Depomed's WO '107 and Rowbotham.**

349. Not only would a person of ordinary skill in the art have been highly motivated to create a controlled release formulation of gabapentin, but such a person would also have had a reasonable expectation of successfully creating such a formulation. (FOF ¶¶ 164-176.)

350. "[O]bviousness cannot be avoided simply by a showing of some degree of unpredictability in the art so long as there was a reasonable probability of success." Pfizer, 480 F.3d at 1364 (reversing district court's finding of nonobviousness of patent claiming salt

form of compound in part because person of skill in the art would reasonably expect claimed salt form would work for intended purpose). In other words, "the expectation of success need only be reasonable, not absolute." Id. (citing Merck & Co., Inc. v. Biocraft Labs., Inc., 874 F.2d 804, 809 (Fed. Cir. 1989); In re O'Farrell, 853 F.2d at 903).

351. One of ordinary skill would have taken gabapentin and put it into one or more of Depomed's WO '107 formulations and they would have had a reasonable expectation that they would have had an efficiently absorbed gastric retained formulation. (FOF ¶ 164.) This reasonable expectation of success stems from the similarities between metformin, as disclosed in Depomed's WO '107, and gabapentin. For example, both drugs had similarity solubility and absorption high in the gastrointestinal tract, and WO '107 disclosed formulations for dugs with these characteristics. (Id.) Both drugs were known to exhibit saturable absorption and it was known that placing such drugs in controlled-release formulations was a known way to avoid saturating the transporter. (FOF ¶ 165.)

352. Furthermore, one of ordinary skill would have had a reasonable expectation of a therapeutic effect for the controlled release formulation as compared to the known immediate release formulation. (FOF ¶ 166.) Therapeutic effect doses, including both 300 mg and 600 mg, were known in the prior art to treat both epilepsy and neuropathic pain. Furthermore, both 300 mg and 600 mg once-daily dose strengths would have been natural starting points for one skilled in the art for creating a once-a-day formulation, as testified to by Dr. Flanagan. (Id.)

353. Depomed's experts attempt to cast doubt on an expectation of success by questioning whether WO '107 discloses a gastric retained dosage form. (FOF ¶¶ 170-171.) Depomed is not permitted to take this position, however, due to equitable principals of judicial estoppel. "The Federal Circuit has established that judicial estoppel is appropriate 'when a party

takes a later position that is inconsistent with a former position.'" MobileMedia Ideas, LLC v. Apple Inc., 907 F. Supp. 2d 570, 623 (D. Del. 2012) (citing Bonzel v. Pfizer, Inc., 439 F.3d 1358, 1362 (Fed.Cir.2006)). WO '107 was filed in the PTO by Depomed and states that the dosage form "is designed for gastric retention." (FOF ¶ 169.) Depomed and the WO '107 inventors had a duty of candor to the PTO. See 37 C.F.R. § 1.68 (requiring each inventor to submit an oath or declaration attesting that "all statements made of the declarant's own knowledge are true and that all statements made on information and belief are believed to be true."). It is unreasonable for Depomed to question the accuracy of statements contained in WO '107 under the circumstances. "Preserving the sworn affidavit preserves the integrity of the PTO and the courts and, therefore, judicial estoppel is appropriate." MobileMedia Ideas, 907 F. Supp. 2d at 623. Further, Depomed incorporated its WO '107 by reference into both the '962 Patent and the Gabapentin Patents as a suitable, gastric retained dosage form for use in the alleged inventions. (JTX 1 at col. 2, l. 52 - col. 3, l. 42; JTX 3 at col. 5, ll. 52-62, col. 6, l. 50 - col. 7, l. 5.)

354. Depomed further attempts to cast doubt on an expectation of success by suggesting that gabapentin's release rate may not avoid saturation of absorption of transporters. (FOF ¶ 174.) These concerns are unfounded and inconsistent with the prior art. (Id.) Even Depomed's expert, Dr. Williams, testified that it was within his skill to modify the release rate of drugs by modifying the amount of swellable hydrophilic polymers in the dosage form and that he had been making these types of modifications to formulations since at least the 1990s. (Id.) Further, a slower rate was known to those of skill in the art to mitigate or overcome any issues associated with saturation of the transporters. (Id.) As Drs. Flanagan and Mayersohn explained, saturable absorption means that only a certain amount of drug can be transported at any given

time and if more drug reaches the transporter after saturation, then the additional drug is not absorbed. (FOF ¶ 132.) As an immediate release formulation releases its entire drug payload at once, there would be more drug competing for the transporters at one time compared to a continuous release over an extended period of time. (FOF ¶ 92.) If anything, one of ordinary skill would have expected a higher bioavailability from a controlled release formulation of gabapentin in comparison to the immediate release formulation. (FOF ¶ 167.) Thus, Depomed's argument is not persuasive.

355. Depomed's suggestion that the Hwang reference (DTX 222) casts doubt on an expectation of success is unfounded because the Hwang reference did not even consider Depomed's own WO '107 prior art. (FOF ¶ 175.)

356. It is perhaps most telling that Depomed failed to put any of the inventors of the Gabapentin Patents or the '962 Patent on the stand. Understanding the inventive process can shed light on "the predictability and expectations in this field of art" and whether the invention was the outcome of an "eureka" moment or whether the inventor merely followed the breadcrumbs laid out in the prior art. Rothman v. Target Corp., 556 F.3d 1310, 1319 (Fed. Cir. 2009). As in Rothman, Dr. Hou's deposition testimony is significant evidence that a person of ordinary skill in the art would have reasonably expected to achieve the claimed features. Depomed did not invent gabapentin and Depomed did not develop its use to treat postherpetic neuralgia. (FOF ¶ 142.) Depomed put a known drug for its known use into the gastric retained formulation that Depomed itself disclosed in WO '107. (FOF ¶ 176.) The Court heard no other testimony from the inventors concerning their inventive process because there was no invention.

357. For at least the reasons stated above, Actavis has established by clear and convincing evidence that gabapentin was a known drug with known properties and known

therapeutic uses, that it was known in the prior art to use dosage forms with swellable polymers to obtain controlled release and gastric retention of soluble drugs with narrow absorption windows and that a person of ordinary skill in the art would have had a reasonable expectation of success putting gabapentin in a prior art dosage form. As the claimed combination of prior art elements were known within the prior art and one or ordinary skill would reasonably had expected the combination of elements to work, claims 17 and 33 of the '927 Patent are invalid as obvious. KSR, 550 U.S. at 421; PharmaStem Therapeutics, 491 F.3d at 1360. The patent is no more than putting a known drug in a known dosage form and, upon administration, getting a known therapeutic benefit.

d) **Asserted Dependent Claims 18, 25, 26, 34, 61 and 62 Would Have Been Obvious in View of Depomed's WO '107 and Rowbotham.**

358. The six asserted claims of the '927 Patent, claims 18, 25, 26, 34, 61 and 62, all depend from either independent claim 17 or claim 33. (FOF ¶ 42.) Thus, the discussion above with respect to claims 17 and 33 applies to claims 18, 25, 26, 34, 61 and 62 as well. (FOF ¶ 178.)

359. Claim 18 of the '927 Patent incorporates the limitations of claim 17, and claim 34 of the '927 patent incorporates the limitations of claim 33. (FOF ¶ 179.) Both claims 18 and 34 further require that "the dosage form is administered once-daily." (Id.) This additional limitation of claims 18 and 34 is described in Depomed's WO '107. (Id.) Accordingly, claim 18 and 34 would have been obvious over the same prior art discussed above with respect to claims 17 and 33.

360. Claim 25 of the '927 Patent incorporates the limitations of claim 17 and further requires that "the gastric retained dosage form release gabapentin to the stomach, duodenum and small intestine." (FOF ¶ 180.) This additional requirement of claim 25 is disclosed in

Depomed's WO '107. (Id.) Thus, claim 25 would have been obvious for these reasons and the reasons discussed above with respect to claims 17 and 33.

361. Claim 26 of the '927 Patent incorporates the limitations of claim 17 and further requires that "the dosage form provides administration of at least 85 wt % of the gabapentin to be delivered over a period of about 5-12 hours." (FOF ¶ 181.) Depomed's WO '107 discloses that a drug is substantially released from the matrix in about eight hours in one instance and further discloses that "[t]hree different dose levels were prepared – systems designed to release 90% of their drug contents at approximately 3 hours, 6 hours and 8 hours, respectively," which was confirmed by in vitro dissolution testing. (Id.) At most, obtaining the release profile set out in claim 26 of the '927 Patent would require no more than routine optimization by one of ordinary skill following the teachings of the prior art given the guidance WO '107 provides to tailor the release profile. (Id.) Thus, claim 26 would have been obvious for these reasons and the reasons discussed above with respect to claims 17 and 33.

362. Claim 61 of the '927 Patent incorporates the limitations of claim 17 and claim 62 of the '927 Patent incorporates the limitations of claim 33. (FOF ¶ 182.) Both claims 61 and 62 further require that "the mammal is a human." (Id.) Depomed's WO '107 discloses that its claimed dosage form is given to patients or subjects in the fed mode and Rowbotham discloses the administration of gabapentin to human patients for the treatment of neuropathic pain. (Id.) In any event, humans are an obvious target for pharmaceutical products. (Id.) Thus, claims 61 and 62 would have been obvious for these reasons and the reasons discussed above with respect to claims 17 and 33.

363. Actavis has therefore established by clear and convincing evidence that all the elements of claims 18, 25, 26, 34, 61 and 62 of the '927 Patent were known or within the

technical grasp of the skilled artisan. KSR, 550 U.S. at 421; PharmaStem Therapeutics, 491 F.3d at 1360.

2. The Asserted Claim of the '989 Patent Would Have Been Obvious in View of Depomed's WO '107 and Rowbotham.

364. Depomed asserted claim 10 of the '989 Patent. (FOF ¶ 43.) Claim 10 depends from claim 1, which is not being asserted in this litigation. (Id.)

365. Claim 10 of the '989 Patent would have been obvious to one of ordinary skill over WO '107 (DTX 234) in view of Rowbotham (DTX 313), along with the knowledge of a person of ordinary skill in the art as evidenced by McLean (DTX 267) and Stevenson (PTX 500).

366. The limitations of claim 1 of the '989 Patent are substantially identical to the limitations found in claim 33 of the '927 Patent. (FOF ¶ 183.) Accordingly, claim 1 of the '989 Patent would have been obvious to one of ordinary skill in the art for the same reasons stated above with respect to claim 33 of the '927 Patent.

367. Claim 10 of the '989 Patent depends from claim 1 and further requires that "gabapentin has a bioavailability greater than or equal to 80% of an equal dose of gabapentin in an immediate release dosage form." (FOF ¶ 184.)

368. Although Depomed's WO '107 does not expressly disclose this limitation, those of skill in the art routinely designed extended release dosage forms to have a bioavailability of at least 80% of an equal dose of the drug in an immediate release dosage form. (FOF ¶ 185.) This is the target of all controlled release dosage forms to ensure that the controlled release dosage form had similar efficacy to multiple dosings of the immediate release dosage forms. (Id.) One skilled in the art would have an expectation that a controlled release form of gabapentin would have at least 80% or more of the bioavailability of an immediate release formulation containing the same amount of gabapentin. (FOF ¶ 186.) As Dr. Flanagan testified, where the

bioavailability is roughly equivalent for the two formulations over the dosing interval, one would expect the therapeutic effect to be equivalent. (FOF ¶ 186.)

369. Drs. Gidal, Felton and Derendorf argue that Actavis has failed to demonstrate that the prior art dosage forms would actually improve the pharmacokinetics of gabapentin and result in a therapeutically effective product. (5/16/2014 Tr. 822:4-10.) But this far exceeds the level of certainty that the law requires. "Obviousness does not require absolute predictability of success," but rather, requires "a reasonable expectation of success." See Medichem, S.A., 437 F.3d at 1165. The testimony of Drs. Gidal, Felton and Derendorf is not probative of whether or not one of ordinary skill in the art would have had such a reasonable expectation of success.

370. For these reasons, and the reasons discussed above with respect to the '927 Patent, claim 10 of the '989 Patent would have been obvious to one of ordinary skill in the art.

371. Actavis has therefore established by clear and convincing evidence that all the elements of claim 10 of the '989 Patent were known or within the technical grasp of the skilled artisan. KSR, 550 U.S. at 421; PharmaStem Therapeutics, 491 F.3d at 1360.

3. The Asserted Claims of the '756 Patent Would Have Been Obvious in View of Depomed's WO '107 and Rowbotham.

372. Depomed asserted claims 1, 2, 5, 6, 7 and 11 of the '756 Patent. (FOF ¶ 189.) Claims 2, 5, 7 and 11, all depend from either independent claims 1 or 6, which themselves do not substantially differ and will be addressed together. (FOF ¶¶ 190, 191.)

373. Claims 1, 2, 5, 6, 7 and 11 of the '756 Patent would have been obvious to one of ordinary skill over Depomed's WO '107 (DTX 234) in view of Rowbotham (DTX 313), along with the knowledge of a person of ordinary skill in the art as evidenced by McLean (DTX 267) and Stevenson (PTX 500). (FOF ¶¶ 195, 201.)

a) **Independent Claims 1 and 6 Would Have Been Obvious in View of Depomed's WO '107 and Rowbotham.**

374. The only claim element claims 1 and 6 of the '756 Patent have that has not been previously discussed for the '927 and '989 Patents, above, is the requirement that "gabapentin is released at a rate sufficient to achieve a lower maximum plasma concentration (C_{max}) compared to an equal dose of gabapentin provided by an immediate release dosage form." (FOF ¶ 191.)

375. Although Depomed's WO '107 does not explicitly state its formulation achieves a reduced C_{max}, those of skill in the art routinely designed controlled release dosage forms to have a lower C_{max} than an immediate release dosage form. (FOF ¶ 192.) One of ordinary skill in the art would have known that lowering C_{max} and extending T_{max} is the natural goal of every controlled release formulation. (FOF ¶ 193.) Modulating the release rate of drugs from a polymeric matrix was a common and routine practice even in the 1990s and obtaining a lower C_{max} would be, at most, a matter of routine optimization for one of ordinary skill in the art. (FOF ¶ 194.)

376. Drs. Gidal, Felton and Derendorf argue that Actavis has failed to demonstrate that the prior art dosage forms would actually improve the pharmacokinetics of gabapentin and result in a therapeutically effective product. (5/16/2014 Tr. 822:4-10.) But this far exceeds the level of certainty that the law requires. "Obviousness does not require absolute predictability of success," but rather, requires "a reasonable expectation of success." See Medichem, S.A., 437 F.3d at 1165. The testimony of Drs. Gidal, Felton and Derendorf is not probative of whether or not one of ordinary skill in the art would have had such a reasonable expectation of success.

377. For these reasons, and the reasons discussed above with respect to the '927 Patent, independent claims 1 and 6 of the '756 Patent would have been obvious to one of ordinary skill in the art.

378. In Purdue II, the Federal Circuit upheld the decision of the Delaware District Court holding two controlled release dosage form patents invalid for obviousness. Purdue II, 377 Fed. App'x at 978. Like claims 1 and 6 of the '756 Patent, the claims in Purdue II also involved claimed pharmacokinetic elements, ones that were broad and "necessarily a characteristic of a one-a-day tramadol formulation." Id. at 983. As Dr. Flanagan testified, the pharmacokinetic element of reduced C_{max} is the natural result of a controlled-release formulation that is releasing its drug slowly and being absorbed slowly. (FOF ¶ 192.)

379. Finding claims 1 and 6 of the '756 Patent obvious is also consistent with the Federal Circuit's holding in In re Cyclobenzaprine Hydrochloride Extended-Release Capsule Patent Litig., 676 F.3d 1063 (Fed. Cir. 2012), cert. denied, 133 S. Ct. 933 (2013) (holding where the relationship between the pharmacokinetics and pharmacodynamics of a drug was not known, there was not a reasonable expectation of success of achieving a specific claimed therapeutically effective, pharmacokinetic profile but noting that the court "do[es] not hold that bioequivalence can never serve as evidence of obviousness. Indeed, it most certainly relevant to that inquiry."). The claims presented in In re Cyclobenzaprine required that the pharmacokinetic profile (i.e., C_{max}, T_{max} and AUC) be tied to therapeutic efficacy, and, in a dependent claim, specified a particular pharmacokinetic profile. Id. at 1066. The Court found that the absence of a known relationship between the pharmacokinetics of the drug and its therapeutic efficacy (the pharmacokinetic – pharmacodynamic or PK/PD relationship) would have foreclosed one of ordinary skill in the art of having a reasonable expectation of success in determining a therapeutically effective pharmacokinetic profile from the prior art. Id. at 1070-71. Further, these claims were directed to an extended release pharmacokinetic profile that went against what one of ordinary skill in the art would expect – the dosage form embodying the claims had a

higher C_{max} and lower C_{min} compared to an immediate release formulation. Id. at 1081-82 ("Cephalon had chosen a PK profile in which the C_{max} rose higher and the minimum blood plasma concentration (C_{min}) dipped lower than those of the immediate-release profile. . . . After reviewing Cephalon's PK profile, Dr. Saks expressed surprise that Cephalon succeeded, because he believed a lower C_{min} would be less effective."). (DTX 323 at 357-58; 5/14/2014 Tr. 695:17-697:11.) And unlike in this case where Depomed presented no inventor testimony regarding the alleged inventions, one of the inventors in In re Cyclobenzaprine testified as to the substantial efforts that were necessary to develop the invention. Id. at 1067, 1072, 1081-82.

380. Unlike In re Cyclobenzaprine, claims 1 and 6 of the '756 Patent require that the ***daily dose*** of gabapentin be ***therapeutically effective***. (FOF ¶¶ 47-49.) Therapeutically effective daily doses of gabapentin for treating postherpetic neuralgia were well-known in the art, however, as described in Rowbotham and McLean. (FOF ¶¶ 124-125.) Furthermore, as Drs. Flanagan and Mayersohn described, the pharmacokinetic parameters recited in the '756 Patent claims are nothing more than the known effect on the pharmacokinetics of a drug when it is put into a controlled release formulation – consistent with what is described in prior art publications such as WO '128 and AB&P. (FOF ¶¶ 192-193; DTX 323 at 357-58.) A person of ordinary skill in the art would have had a reasonable expectation of producing a therapeutically effective, gastric retained dosage form having these broad pharmacokinetic parameters when it contained the known, effective dose of gabapentin, as Dr. Flanagan testified. (FOF ¶ 194.) It was even within the skill of Depomed's expert, Dr. Williams, to modify the release rate of drugs by modifying the amount of swellable hydrophilic polymers in the dosage form, which would modify its pharmacokinetic profile, since at least the 1990s. (Id.)

381. For these reasons, and the reasons discussed above with respect to the '927 Patent, independent claims 1 and 6 of the '756 Patent would have been obvious to one of ordinary skill in the art.

382. Actavis has therefore established by clear and convincing evidence that all the elements of claims 1 and 6 of the '756 Patent were known or within the technical grasp of the skilled artisan. KSR, 550 U.S. at 421; PharmaStem Therapeutics, 491 F.3d at 1360.

b) **Dependent Claims 2, 5, 7 and 11 Would Have Been Obvious in View of Depomed's WO '107 and Rowbotham.**

383. The four additional asserted claims of the '756 Patent, claims 2, 5, 7 and 11, all depend from either independent claims 1 or 6. (FOF ¶ 196.) Thus, the discussion above with respect to claims 1 and 6 applies to claims 2, 5, 7 and 11. (Id.)

384. Claim 2 of the '756 Patent incorporates the limitations of claim 1, and claim 7 of the '756 Patent incorporates the limitations of claim 6. (FOF ¶ 197.) Both claims 2 and 7 further require that "the time to reach maximum plasma concentration is longer relative to the time to reach maximum plasma concentration from an immediate release dosage form comprising the dose of gabapentin." (Id.)

385. This additional limitation of claims 2 and 7 is nothing more than a natural result of a controlled-release formulation releasing the drug more slowly than an immediate-release formulation. (FOF ¶ 198.) Thus, claims 2 and 7 would have been obvious over the same prior art discussed above with respect to claims 1 and 6.

386. Claim 5 of the '756 Patent incorporates the limitations of claim 1 and further requires that the dosage form comprise "a dose of gabapentin of between about 300-600 mg." (FOF ¶ 199.) The prior art discloses therapeutically effective doses from 300 to 4,800 mg of gabapentin to treat epilepsy or neuropathic pain and both 300 mg and 600 mg once-daily dose

strengths would have been natural starting points for one skilled in the art for creating a once-a-day formulation, as testified to by Dr. Flanagan. (Id.) Thus, claim 5 would have been obvious over the same prior art discussed above with respect to claims 1 and 6.

387. Claim 11 of the '756 Patent incorporates the limitations of claim 6 and further requires that "the condition is neuropathic pain." (FOF ¶ 200.) One of ordinary skill in the art in October 2001 knew that gabapentin was used to treat neuropathic pain. (Id.) The use of gabapentin is merely the use of a known drug for one of its known purposes – i.e., as a treatment of neuropathic pain. (Id.) Thus, claim 11 would have been obvious over the same prior art discussed above with respect to claims 1 and 6.

388. Actavis has therefore established by clear and convincing evidence that all the elements of claims 2, 5, 7 and 11 of the '756 Patent were known or within the technical grasp of the skilled artisan. KSR, 550 U.S. at 421; PharmaStem Therapeutics, 491 F.3d at 1360.

4. The Asserted Claims of the '332 and '992 Patent Would Have Been Obvious to One of Ordinary Skill in the Art.

389. Depomed asserted claims 1, 6, 17, 22 and 24 of the '332 Patent and claims 1, 5 and 22 of the '992 Patent. (FOF ¶¶ 202, 204.) Claim 6 of the '332 Patent depends from claim 1 and claim 17 depends from unasserted claim 12. (FOF ¶ 202.) Claim 5 of the '992 Patent depends from claim 1. (FOF ¶ 205.)

390. Of the four independent claims of the '332 Patent at issue, claims 1, 12, 22 and 24 differ only in that claims 12 and 24 are directed towards a method of treatment, claims 1 and 12 are directed to achievement of a lower C_{max} as compared to claims 22 and 24 that are directed to a longer T_{max}, and claim 22 has a further limitation of a gabapentin dose range of 300-600 mg. (FOF ¶ 203.)

391. Claims 1 and 22 of the '992 Patent only differ from claims 1 and 24 of the '332 Patent in that they require administration to a human subject. Because all these independent claims of the '332 and '992 Patents are essentially identical, they are discussed together. (FOF ¶ 205.)

a) **Independent Claims 1, 12, 22 and 24 of the '332 Patent and Claims 1 and 22 of the '992 Patent Would Have Been Obvious in View of Depomed's WO '107 and Rowbotham.**

392. Independent claims 1, 12, 22 and 24 of the '332 Patent and claims 1 and 22 of the '992 Patent would have been obvious to one of ordinary skill over Depomed's WO '107 (DTX 234) in view of a Rowbotham (DTX 313) for the same reasons as discussed above for the '927, '989 and '756 Patents.

393. Each of the '332 and '992 claims require that the bioavailability of gabapentin be at least 80% of that provided by the immediate release when measured by the AUC_{inf}. (FOF ¶ 207.) The claims then also require either a lower C_{max} or a higher T_{max}. (Id.)

394. Although Depomed's WO '107 does not expressly disclose these pharmacokinetic limitations, those of skill in the art routinely designed controlled release dosage forms to have a lower C_{max} than an immediate release dosage form, a longer T_{max} and an equivalent AUC_{inf}. (FOF ¶ 208.) As explained above, one of ordinary skill in the art would have known that lowering C_{max} and extending T_{max} while maintaining an equivalent AUC_{inf} is the natural goal of every controlled release formulation. (FOF ¶ 209.) Modulating the release rate of drugs from a polymeric matrix was a common and routine practice even in the 1990s and obtaining a lower C_{max} would be, at most, a matter of routine optimization for one of ordinary skill in the art. (FOF ¶ 194.)

395. Dr. Gidal argues that Actavis has failed to demonstrate that the prior art dosage forms would actually improve the pharmacokinetics of gabapentin and result in a therapeutically

effective product. (5/16/2014 Tr. 822:4-10.) But this far exceeds the level of certainty that the law requires. "Obviousness does not require absolute predictability of success," but rather, requires "a reasonable expectation of success." See Medichem, S.A., 437 F.3d at 1165. The testimony of Dr. Gidal is not probative of whether or not one of ordinary skill in the art would have had such a reasonable expectation of success.

396. Just as with the '756 Patent, finding claims 1, 12, 22 and 24 of the '332 Patent and claims 1 and 22 of the '992 Patent is consitent with Purdue II and In re Cyclobenzaprine. (See, *supra*, ¶¶ 378-380.) Unlike in In re Cyclobenzaprine, the '332 Patent and '992 Patent claims requiring theraputic effecitiveness, claims 12 and 24 of the '332 Patent and claim 22 of the '992 Patent, require that the ***dose*** of gabapentin be ***therapeutically effective***. (FOF ¶¶ 53, 56, 60.) Therapeutically effective daily doses of gabapentin for treating postherpetic neuralgia were well-known in the art, however, as described in Rowbotham and McLean. (FOF ¶¶ 124-125.) Furthermore, as Drs. Flanagan and Mayersohn described, the pharmacokinetic parameters recited in the '332 Patent and '992 Patent claims are nothing more than the known effect on the pharmacokinetics of a drug when it is put into a controlled release formulation – consistent with what is described in prior art publications such as WO '128 and AB&P. (FOF ¶¶ 192-193; DTX 323 at 357-58.) A person of ordinary skill in the art would have had a reasonable expectation of producing a therapeutically effective, gastric retained dosage form having these broad pharmacokinetic parameters when it contained the known, effective dose of gabapentin, as Dr. Flanagan testified. (FOF ¶ 194.) It was even within the skill of Depomed's expert, Dr. Williams, to modify the release rate of drugs by modifying the amount of swellable hydrophilic polymers in the dosage form, which would modify its pharmacokinetic profile, since at least the 1990s. (Id.)

397. For these reasons, and the reasons discussed above with respect to the '927, '989 and '756 Patents, independent claims 1, 12, 22 and 24 of the '332 Patent and independent claims 1 and 22 of the '992 Patent would have been obvious to one of ordinary skill in the art. See Purdue II, 377 Fed. App'x at 978.

398. Actavis has therefore established by clear and convincing evidence that all the elements of claims 1, 12, 22 and 24 of the '332 Patent and claims 1 and 22 of the '992 Patent were known or within the technical grasp of the skilled artisan. KSR, 550 U.S. at 421; PharmaStem Therapeutics, 491 F.3d at 1360.

b) **Independent Claims 1, 12, 22 and 24 of the '332 Patent and Claims 1 and 22 of the '992 Patent Would Have Been Obvious In View of WO '128 and Rowbotham.**

399. Independent claims 1, 12, 22 and 24 of the '332 Patent and claims 1 and 22 of the '992 Patent would have been obvious to one of ordinary skill over WO '128 (DTX 236) in view of Rowbotham (DTX 313).

400. Claims 12 and 24 of the '332 Patent and claim 24 of the '992 Patent all are directed to a "method of treating a condition responsive to a therapeutic dose of gabapentin." (FOF ¶¶ 50-60.) Rowbotham discloses doses of gabapentin to treat neuropathic pain. (FOF ¶ 212.)

401. The independent claims all require either "a dosage form" or "orally administering a dosage form." (FOF ¶¶ 50-60.) WO '128 is directed to "a new dosage form for highly water soluble medicaments." (FOF ¶ 213.)

402. The independent claims all require "a matrix comprising gabapentin." (FOF ¶¶ 50-60.) WO '128 states that "[i]n a controlled release dosage form, the formulator tries to reduce the rate of dissolution by, for example, embedding the drug in a polymeric matrix." (FOF ¶ 215.)

403. The independent claims all require "upon ingestion of the dosage form gabapentin is released from the matrix into the upper gastrointestinal tract over about 5-12 hours." (FOF ¶¶ 50-60.) WO '128 discloses its dosage form "allowing sustained delivery of contained drug to absorption sites in the upper gastrointestinal tract." (FOF ¶ 213.) In Example 3, WO '128 discloses its controlled release formulation having a T_{max}, the time to reach maximum plasma concentration, as 5 hours. (FOF ¶ 217.)

404. The independent claims all require "a rate sufficient to achieve a lower maximum plasma concentration than that provided by an immediate release dosage form comprising an equal amount of gabapentin." (FOF ¶¶ 50-60.) In Example 3, WO '128 discloses its controlled release formulation having a C_{max}, the maximum plasma concentration, lower than that of the immediate release formulation. (FOF ¶ 217.)

405. The independent claims all require "bioavailability of gabapentin is at least 80% of that provided by the immediate release dosage form comprising an equal amount of gabapentin as measured by the area under the plasma concentration-time curve, $AUC_{inf.}$" (FOF ¶¶ 50-60.) WO '128 states that there is "no impact on bioavailability." (FOF ¶ 217 (WO '128's Example 5).)

406. One of ordinary skill in the art would be motivated to combine WO '128 and Rowbotham. Generally, "[c]ontrolled release delivery systems are known to offer advantages over conventional dosage forms, including increased patient compliance with prescriptions, decreased total drug delivery, and decreased side effects." Purdue I, 642 F. Supp. 2d at 336; see also Alza II, 464 F.3d at 1286.

407. Although WO '128 does not explicitly mention gabapentin, one of ordinary skill in the art would have been motivated to formulate gabapentin in the WO '128 gastric retained

dosage form to alleviate the burden on patients to take multiple doses per day, improve patient compliance, and reduce the incidence of side effects. (FOF ¶ 151.)

408. One of ordinary skill in the art would have known that gabapentin was not suitable for a conventional controlled-release dosage form and that the only viable approach to making a controlled-release form of gabapentin would be to use a gastric retentive system in order to hold the gabapentin in a place above its window of absorption for an extended period of time. (FOF ¶ 152.) Named inventor, Dr. Hou, confirmed that it was gabapentin's known absorption characteristics that made it such a good candidate for a gastric retained controlled-release dosage form. (FOF ¶ 153.)

409. One of ordinary skill in the art would have been motivated to use the dosage form disclosed in WO '128 because those formulations were ideal for drugs of "high water solubility and a limited window of absorption." (FOF ¶ 213.) One of ordinary skill in the art would have been further motivated to replace the metformin as disclosed in WO '128 with gabapentin because both drugs were known to exhibit saturable absorption high in the gastrointestinal tract. (FOF ¶ 218.) This is because a controlled-release gastric retained dosage form would improve issues relating to saturation. (Id.)

410. Depomed's experts rehash many of the same arguments discussed above with respect to motivation to combine Depomed's WO '107 with Rowbotham. For the same reasons discussed above, those arguments are without merit.

411. Actavis has therefore established by clear and convincing evidence that a person of ordinary skill in the art would recognize that the controlled release, gastric retained formulations disclosed in WO '128 would improve gabapentin absorption and pharmacokinetics in the same way those formulations improved other highly water soluble drugs. (FOF ¶ 217.)

Metformin and gabapentin share properties relevant to their absorption by the human body after ingestion – namely, high water solubility, a narrow window of absorption in the upper GI tract and absorption via a saturable transporter. (FOF ¶ 218.) Therefore, gabapentin, just like metformin, would have been well suited to a gastric retained, controlled release formulation. (Id.) Simply put, it was obvious to try gabapentin in the prior-art, controlled release formulations for metformin.

412. Although WO '128 does not provide pharmacokinetic data for gabapentin, one of ordinary skill in the art would have had a reasonable expectation of success in combining WO '128 and Rowbotham. (FOF ¶ 219.) Gabapentin, having the important characteristics of absorption in common with metformin would allow one of ordinary skill in the art to reasonably expect that gabapentin would exhibit the pharmacokinetic trends of metformin in the WO '128 dosage form, namely a lower $C_{max,}$ higher T_{max} and equivalent AUC_{inf}. (Id.) For example, both drugs had similarity solubility and absorption high in the gastrointestinal tract and WO '128 disclosed formulations for dugs with these characteristics. (Id.) Both drugs were known to exhibit saturable absorption and it was known that placing such drugs in controlled-release formulations was a known way to avoid saturating the transporter. (Id.)

413. Furthermore, one of ordinary skill would have had a reasonable expectation of a therapeutic effect for the controlled release formulation as compared to the known immediate release formulation. (FOF ¶ 167.) Therapeutic effect doses, including both 300 mg and 600 mg, were known in the prior art to treat both epilepsy and neuropathic pain. (Id.) Furthermore, both 300 mg and 600 mg once-daily dose strengths would have been natural starting points for one skilled in the art for creating a once-a-day formulation, as testified to by Dr. Flanagan. (Id.)

414. For at least the reasons stated above, Actavis has established by clear and convincing evidence that gabapentin was a known drug with known properties and known therapeutic uses, that it was known in the prior art to use dosage forms with swellable polymers to obtain controlled release and gastric retention of soluble drugs with narrow absorption windows and that a person of ordinary skill in the art would have had a reasonable expectation of success putting gabapentin in a prior art dosage form. As the claimed combination of prior art elements were known within the prior art and one or ordinary skill would reasonably had expected the combination of elements to work, independent claims 1, 12, 22 and 24 of the '332 Patent and claims 1 and 22 of the '992 Patent are invalid as obvious. KSR, 550 U.S. at 421; PharmaStem Therapeutics, 491 F.3d at 1360.

415. Actavis has therefore established by clear and convincing evidence that all the elements of claims 1, 12, 22 and 24 of the '332 Patent and claims 1 and 22 of the '992 Patent were known or within the technical grasp of the skilled artisan. KSR, 550 U.S. at 421; PharmaStem Therapeutics, 491 F.3d at 1360.

c) **Dependent Claims 6 and 17 of the '332 Patent and Claim 5 of the '992 Patent Would Have Been Obvious In View of Rowbotham and Depomed's WO '107 or WO '128.**

416. Claim 6 of the '332 Patent depends from claims 1, 4 and 5 of the '332 Patent and Claim 17 of the '332 Patent depends from claim 12 of the '332 Patent. (FOF ¶¶ 52, 54.) Claim 5 of the '992 Patent depends from claims 1and 4of the '992 Patent. (FOF ¶ 52.) Thus, the discussion above with respect to claims 1 and 12 of the '332 Patent and claim 1 of the '992 patent applies to claims 6 and 17 of the '332 Patent and claim of the '992 Patent.

417. Claim 6 of the '332 Patent and claim 5 of the '992 Patent both further require "the matrix is a polymer matrix" and "the polymer matrix is comprised of a swellable, hydrophilic polymer." (FOF ¶ 52.) Claim 6 of the '332 Patent further requires "the gabapentin is released

from the polymer matrix by diffusion." (Id.) WO '128 discloses a polymer matrix and a polymer matrix that is comprised of a swellable, hydrophilic polymer. (FOF ¶¶ 223-224.) WO '128 further discloses the "drug must diffuse to be released for absorption." (FOF ¶ 215.) Thus, claim 6 of the '332 Patent and claim 5 of the '992 Patent would have been obvious over the same prior art discussed above with respect to claims 1 of the '332 Patent and claim 1 of the '992 Patent.

418. Claim 17 of the '332 Patent further requires "the condition treated in the method is neuropathic pain." (FOF ¶ 54.) Rowbotham discloses administering a therapeutically effective dose of gabapentin to treat neuropathic pain. (FOF ¶ 212.) Thus, claim 17 of the '332 Patent would have been obvious over the same prior art discussed above with respect to claim 12 of the '332 Patent.

419. Actavis has therefore established by clear and convincing evidence that all the elements of claims 6 and 17of the '332 Patent and claim 5 of the '992 Patent were known or within the technical grasp of the skilled artisan. KSR, 550 U.S. at 421; PharmaStem Therapeutics, 491 F.3d at 1360.

5. Depomed's Evidence of Secondary Considerations Does Not Outweigh the Strong Showing of Obviousness.

420. Depomed argues a few secondary considerations of nonobviousness in an attempt to defeat the *prima facie* obviousness of the asserted claims. In particular for the Gabapentin Patents, Depomed argues that Gralise's supposed commercial success, copying of the patents, an alleged long-felt but unmet need for a controlled release formulation of gabapentin and the skepticism and failure of others to demonstrate that the claimed invention is not obvious. For the '962 Patent, Depomed only argues there was a long felt need for an improved, gastric retained

dosage form. Depomed is mistaken; it has failed to demonstrate that any of these considerations exist or are even applicable.

421. "The rationale for giving weight to the so-called 'secondary considerations' is that they provide objective evidence of how the patented device is viewed in the marketplace, by those directly interested in the product." Demaco Corp. v. F. Von Langsdorff Licensing Ltd., 851 F.2d 1387, 1391 (Fed. Cir. 1988) (citing Graham v. John Deere Co., 383 U.S. 1, 35-36 (1966)). Depomed bears the burden of establishing a nexus between the evidence presented and the merits of the claimed invention. In re GPAC Inc., 57 F.3d 1573, 1580 (Fed. Cir. 1995); In re Paulsen, 30 F.3d 1475, 1482 (Fed. Cir. 1994). In other words, to be relevant to the obviousness analysis, the existence of any secondary consideration must be a result of the merits of the claimed invention. Depomed has no reliable or relevant evidence of secondary considerations of nonobviousness.

422. Moreover, even when present, secondary considerations do not control the obviousness determination. Stamps.com Inc. v. Endicia, Inc., 437 F. App'x 897, 905 (Fed. Cir. 2011). Even substantial secondary indicia of non-obviousness cannot save an obvious invention. Leapfrog Enters., Inc. v. Fisher-Price, Inc., 485 F.3d 1157, 1162 (Fed. Cir. 2007); Pfizer, 480 F.3d at 1372; Ryko Mfg. Co. v. Nu-Star, Inc., 950 F.2d 714, 719 (Fed. Cir. 1991). Thus, even if Depomed had met its burden of proof on any of these secondary considerations, none of them is sufficient, either individually or collectively, to overcome the strong *prima facie* case of obviousness. In fact, the evidence makes clear that the claimed invention of the asserted claims does not impart any unique or unexpected benefit that the prior art failed to provide.

423. In view of strong showing of obviousness, no secondary considerations can overcome Actavis' *prima facie* showing of obviousness. The Gabapentin Patents are no more

than putting a known drug in a known dosage form and, upon administration, getting the same extended release and a known therapeutic benefit.

a) **No Skepticism or Failure of Others**

424. Depomed has not established that others failed to make a gastric retained dosage form of gabapentin. "Absent a showing of long-felt need or the failure of others, the mere passage of time without the claimed invention is not evidence of nonobviousness." Iron Grip Barbell Co., Inc. v. USA Sports, Inc., 392 F.3d 1317, 1325 (Fed. Cir. 2004).

425. Warner-Lambert's only attempt at making a sustained release formulation of gabapentin was non-gastric retained formulation in the mid-1980s, it was known that gabapentin was absorbed only in the upper gastrointestinal tract. (FOF ¶¶ 229, 230.) Warner-Lambert's single study, therefore, was not a failure to make a gastric retained dosage form of gabapentin. Rather, this study led to the knowledge that gabapentin had a narrow window of absorption in the upper gastrointestinal tract. (FOF ¶ 230.) Lambert's failure to develop an extended-release gabapentin product may be a result of a business strategy rather than a technical inability to formulate one. (FOF ¶ 233.)

426. Nor were Warner-Lambert's single meetings with the "French company" and ALZA an attempt to develop a controlled release formulation of any kind. The one meeting with the French company was simply to gain knowledge on a gastric retained dosage form that the French company purported to work in the fasted or fed state. This was of particular interest to Warner-Lambert as Neurontin was approved to be taken with or without food. (FOF ¶ 231.) Similarly, the one cursory meeting with ALZA does not constitute an attempt to develop a controlled release formulation of gabapentin as the ALZA formulation was that of an osmotic pump. (FOF ¶ 232.) The skepticism of Pfizer was of the osmotic pump dosage form, a dosage form that does not swell, and not of a controlled-release gabapentin dosage form. (Id.)

427. Nor do the experiments of pharmaceutical company Andrx demonstrate that Andrx was attempting to make a gastric retentive dosage form of gabapentin. Both the formulation and the test conditions show that the formulation was not a gastric retained dosage form. (FOF ¶ 234.) Further, Andrx was aware that gabapentin was largely absorbed in the upper gastrointestinal tract and, therefore, a traditional controlled release formulation made little sense to try. (See id.) The more likely explanation is that Andrx was testing a platform for use with their patented gabapentin prodrug.

428. Depomed also failed to establish that XenoPort tried and failed to make a gastric retained formulation for gabapentin as there is no evidence that XenoPort even tried such a formulation. (FOF ¶ 235.) In fact, XenoPort's business model is focused on the development of prodrugs. (Id.)

429. Depomed's claims that two of these companies "failed" while using a traditional sustained release dosage form for gabapentin, despite those companies' knowledge that gabapentin is absorbed only in the upper gastrointestinal tract, and the other without any actual attempts to develop a dosage form. (FOF ¶¶ 234, 235.) The evidence does not suggest, however, that these companies had the goal of creating a gastric retained, controlled release gabapentin formulation. (FOF ¶¶ 234, 235.) Thus, the evidence does not show that these so-called attempts "failed" because the dosage form lacked the claimed features. See, e.g., Ormco Corp. v. Align Tech., Inc., 463 F.3d 1299, 1313 (Fed. Cir. 2006) (finding no suggestion that "prior attempts failed because the devices [at issue] lacked the claimed features"). Depomed's experts, lacking any relevant foundation for their claims, fail to establish any skepticism in the industry or failed attempts.

b) **No Long-felt But Unmet Need**

430. Depomed has failed to establish any long-felt unmet need for both the Gabapentin Patents and the '962 Patent. Depomed's experts fail to demonstrate any long-felt need or that the patents met any alleged long-felt need. (FOF ¶¶ 237-242.)

431. [redacted]

432. For the Gabapentin Patents, Dr. Brown, who does not consider herself as one of ordinary skill in the art, admits she prescribes Lyrica to patients more often than Gralise if an immediate release gabapentin is not successful. (FOF ¶¶ 237, 239.) She also admits that she did not consider whether the prior art would have met any need that existed at that time. (FOF ¶ 238.) As explained by Dr. Sinatra, there are no compliance problems for patients with postherpetic neuralgia taking immediate release gabapentin because, unlike medications used for treating undetectable symptoms such as high blood pressure, a patient being treated for pain would not forget to take their pain medication. (FOF ¶ 240.)

433. In addition, the commercial performance of Gralise does not reflect the existence of a long-felt need prior to its launch. (FOF ¶¶ 247-254.) Gralise sales performance pale in comparison to competing products such as Neurontin, which was a blockbuster drug. (FOF ¶ 250.) This indicates that Gralise did not meet a long-felt, unmet need.

c) **No Copying**

434. Depomed has failed to establish any copying. (FOF ¶ 243.) The Actavis ANDA Products were not designed to be a copy of Gralise and design decisions were made before

Gralise was commercially available. (FOF ¶ 244.) Although Actavis' gabapentin once daily project was of high importance due to the possibility of receiving marketing exclusivity from FDA, Dr. Venugopal explains that every first-to-file opportunity was considered a high priority at Actavis. (FOF ¶ 246.) Regardless, copying "is not compelling evidence of non-obviousness in the Hatch-Waxman context due to the unique nature of the ANDA process." Allergan, Inc. v. Watson Laboratories, Inc.-Florida, slip op., Case No. 09-511, 2012 WL 1133684, at *25 (D. Del., March 31, 2012) (citation omitted); see also Purdue II, 377 Fed. App'x at 983 ("[W]e do not find compelling Purdue's evidence of copying in the ANDA context where a showing of bioequivalency is required for FDA approval."); Santarus Inc. v. Par Pharm., Inc., 720 F. Supp. 2d 427, 458 (D. Del. 2010). This case is no exception.

d) **No Commercial Success**

435. Depomed cannot overcome Actavis' showing of obviousness based on any argument that Gralise is allegedly a commercial success. "[T]he law deems evidence of (1) commercial success, and (2) some causal relation or 'nexus' between an invention and commercial success of a product embodying that invention, probative of whether an invention was non-obvious." Merck & Co., Inc. v. Teva Pharms. USA, Inc., 395 F.3d 1364, 1376 (Fed. Cir. 2005); see also GPAC, 57 F.3d at 1580-81 (citing Demaco, 851 F.2d at 1392) (concluding that the patentee had not met its burden to demonstrate that the commercial success "resulted directly from the subject matter claimed in the [patent-in-suit]"). It is well settled, however, that "a 'nexus must be established between the merits of the claimed invention and evidence of commercial success before that evidence may become relevant to the issue of obviousness.'" Iron Grip Barbell, 392 F.3d at 1324 (citation omitted).

436. [redacted]

[redacted]

437. [redacted]

[redacted]

438. [redacted]

[redacted]) In situations such as this, where there are multiple patents covering a product, no presumption of nexus is appropriate. Therasense, Inc. v. Becton, Dickson & Co., 593 F.3d 1289, 1299 (Fed. Cir. 2010),

reh'g en banc granted, opinion vacated, 374 F. App'x 35 (Fed. Cir. 2010), opinion reinstated in relevant part, 649 F.3d 1276 (Fed. Cir. 2011).

439. [redacted] "The mere fact that generic pharmaceutical companies seek approval to market a generic version of a drug, without more, is not evidence of commercial success that speaks to the non-obviousness of patent claims." Galderma Labs., 737 F.3d at 740. The fact that an ANDA applicant might "believe[] that it can make a profit selling a generic version of the claimed invention . . . tells us very little about the level of commercial success of the patented invention relative to the prior art." Id. Nor does it inform "the extent to which the [alleged] commercial success of the branded drug is 'due to the merits of the claimed invention beyond what was readily available in the prior art.' As such, it does not support a finding of non-obviousness." Id. (citation omitted).

440. [redacted] Where the alleged success could just as easily be attributed to marketing power or capabilities, even if it is "found that the claimed invention was a 'commercial success,' this evidence does not convince us that the invention was not obvious." Richardson-Vicks, 122 F.3d at 1484 (recognizing that the advantages of the active ingredient "were well known by doctors and patients alike"); see also In re DBC, 545 F.3d 1373, 1384 (Fed. Cir. 2008).

II. THE ASSERTED CLAIMS OF THE '962 PATENT ARE INVALID AS OBVIOUS

A. The Asserted Claims of the '962 Patent Would Have Been Obvious in View of Depomed's WO '107.

441. Depomed asserted claims 5, 8, 10 and 13 of the '962 Patent. (FOF ¶ 255.) All of the asserted claims are invalid as obvious over Depomed's WO '107 along with the knowledge of a person of ordinary skill in the art.

442. Claim 1 of the '962 Patent is directed to a "controlled-release oral drug dosage form for releasing a drug into at least a portion of a region defined by the stomach and the upper gastrointestinal tract." (FOF ¶ 31.) WO '107 discloses controlled-release oral drug dosage form that is "retained in the stomach for an extended period of time" and provides "multi-hour, controlled delivery of the drug into the stomach." (FOF ¶ 256.)

443. Claim 1 of the '962 Patent further requires "a solid monolithic matrix with said drug contained therein." (FOF ¶ 31.) The dosage form of WO '107 is "a formulation in which the drug is dispersed in a polymeric matrix that is water-swellable" and formed by compression. (FOF ¶ 256.) This is a common method that is known in the art to make a monolithic polymeric matrix containing a drug. (FOF ¶ 257.)

444. Claim 1 of the '962 Patent further requires the "matrix being non-circular in shape and having first and second orthogonal axes of unequal length." (FOF ¶ 31.) Depomed's WO '107 discloses dosage forms that are non-circular in shape, having dimensions of an "elongated tablet with dimensions 18 to 22 mm in length, 6.5 to 7.8 mm in width, and 6.2 to 7.5 mm in height," and states that a "preferred set of dimensions is 20 mm in length, 6.7 mm in width, and 6.4 mm in height." (FOF ¶ 258.) The ranges specified for each dimension are not equal – disclosing to one of ordinary skill in the art that none of the three dimensions should be identical. (Id.)

445. Claim 1 of the '962 Patent further requires the "matrix being one that swells in an unrestricted manner along both such axes upon imbibition of water." (FOF ¶ 31.) Depomed's WO '107 discloses "a polymeric matrix that is water-swellable" and that the polymeric matrix "(i) swells . . . to a size large enough to cause it to be retained in the stomach during the fed mode." (FOF ¶ 256.) As Flanagan testified, the polymers in the matrix swell to several times their original volume and the dosage form swells to at least twice its original size upon ingestion. (Id.)

446. Claim 1 of the '962 Patent further requires the "longer such axis having a maximum length of 3.0 cm when said matrix is unswollen." (FOF ¶ 31.) Depomed's WO '107 discloses an "elongated tablet with dimensions 18 to 22 mm in length, 6.5 to 7.8 mm in width, and 6.2 to 7.5 mm in height," and "a maximum length of 3.0 cm when said matrix is unswollen." (FOF ¶ 258.) In any event, setting a maximum unswollen dimension of 3.0 cm for an oral dosage form is nothing more than common sense because a tablet that exceeds this size (about 1.2 inches) would be very uncomfortable and nearly impossible for many people to swallow. (Id.)

447. Claim 1 of the '962 Patent further requires "the shorter such axis achieving a minimum length of 1.2 cm within one hour of immersion of said dosage form in water." (FOF ¶ 31.) Dr. Flanagan testified that creating a gastric retained dosage form of a specific swollen size, i.e. one large enough to remain in the stomach during fed mode, would be well within the purview of the knowledge of one skilled in the art with routine testing. (FOF ¶ 260.) The types of sizes that would be gastric retained because they resist expulsion from the stomach were well known in the art. (Id.) For example, WO '128 explains that "where Caldwell describes a device that when it reaches the stomach, it becomes a minimum size of

1.6 centimeters and it can have a maximum size of five centimeters so it will not pass from the stomach through the pylorus." (Id.) Thus, those of ordinary skill in the art would understand that the dosage form should be dimensioned and swellable polymers should be selected such that the swollen tablet would reach a minimum size of, e.g., 1.2 cm quickly to avoid passing from the stomach through the pylorus. (Id.)

448. Claim 1 of the '962 Patent further requires "matrix has a shape which when projected onto a plane, is either an oval or a parallelogram." (FOF ¶ 31.) Although Depomed's WO '107 does not specifically disclose an oval tablet, it further states that an elongated tablet, as described in its examples, is not the only shape that this dosage form can take. (FOF ¶ 259.) Oval tablets had been routinely used in the prior art. (Id.) One such example, International Publication No. WO 98/56360 ("WO '360"), discloses a "pharmaceutical formulation in a generally oval shape including, but not limited to, oval, modified oval and caplet-shaped form." (Id.) The shape of the tablet and the various dimensions set forth in the '962 Patent would have been simple design choices to one of skill in the art. (FOF ¶ 261.)

449. Dependent claims 5, 8, and 10 depend from claim 1and dependent claim 13 depends from claim 10. (FOF ¶ 32, 33.) Thus, the discussion above with respect to claims 1 applies to claims 5, 8, 10 and 11 as well. Given the finite number of identified, predictable solutions regarding tablet shape and size, choosing an oval or parallelogram tablet of the dimensions recited in the '962 Patent would have been obvious to try. Hoffmann-La Roche, 2014 WL 1394948 at *6.

450. Claims 5 and 8 of the '962 Patent incorporate the limitations of claim 1 of the '962 Patent and further require that the "shorter axis has a length of 0.7 cm to 1.5 cm when said matrix is unswollen" and that the "longer axis has a maximum length of 2.5 cm when said matrix

is unswollen," respectively. (FOF ¶ 32.) Depomed's WO '107 discloses dosage forms having dimensions of an "elongated tablet with dimensions 18 to 22 mm in length, 6.5 to 7.8 mm in width, and 6.2 to 7.5 mm in height," and states that a "preferred set of dimensions is 20 mm in length, 6.7 mm in width, and 6.4 mm in height." (FOF ¶ 258.) In any event, the shape of the tablet and the various dimensions set forth in the '962 Patent would have been obvious design choices to one of skill in the art. (FOF ¶ 261.) Dr. Flanagan testified it is "very common for one skilled in the art to be selecting different sizes and shapes of tablets, so [shape] would be just a design choice." (Id.) Accordingly, claims 5 and 8 would have been obvious over the same prior art discussed above with respect to claim 1.

451. Claim 10 and 13 of the '962 Patent incorporate the limitations of claim 1 of the '962 Patent and further require that the "matrix is a water-swellable polymer" and that the "water-swellable polymer is a member selected from the group consisting of poly(ethylene oxide), hydroxypropylmethyl cellulose, and hydroxyethyl cellulose," respectively. (FOF ¶ 32-33.) As mentioned previously, WO '107 discloses "a polymeric matrix that is water-swellable." (FOF ¶ 256.) Depomed's WO '107 further discloses suitable polymers including poly(ethylene oxide), hydroxymethylcellulose and hydroxyethylcellulose. (FOF ¶ 103.) Accordingly, claims 10 and 13 would have been obvious over the same prior art discussed above with respect to claim 1.

452. Actavis has therefore established by clear and convincing evidence that WO '107 disclosed or suggested each and every claim limitation of the asserted claims of the '962 Patent and that given the finite number of identified, predictable solutions regarding tablet shape and size, choosing an oval or parallelogram tablet of the dimensions recited in the '962 Patent would have been obvious to try. Hoffmann-La Roche, 2014 WL 1394948 at *6.

453. Actavis has therefore established by clear and convincing evidence that all the elements of claims 5, 8, 10 and 13 of the '962 Patent were known or within the technical grasp of the skilled artisan. KSR, 550 U.S. at 421; PharmaStem Therapeutics, 491 F.3d at 1360.

B. Secondary Considerations Do Not Overcome the Obviousness of the Asserted Claims of the '962 Patent.

454. Depomed failed to demonstrate that the '962 Patent met a long-felt need. (FOF ¶ 273.) Dr. Hopfenberg testified that the key improvements of the '962 Patent over the '475 and '280 Patents was the claimed dosage forms ability to swell to a minimum length of 1.2 cm within one hour of immersion and that its shape when projected be either an oval or parallelogram. (FOF ¶ 270.) This does not overcome the strong *prima facie* case of obviousness against the '962 Patent. See Leapfrog Enters., Inc., 485 F.3d at 1162; Pfizer, 480 F.3d at 1372; Ryko Mfg. Co. v. Nu-Star, Inc., 950 F.2d at 719. In fact, Dr. Hopfenberg stated that as of 2012 there was still a long felt need for improved, gastric retained dosage forms. (Id.) Therefore, if there even was such a long-felt need, the '962 Patent failed to meet such a need.

455. Further and for the same reasons discussed above for the Gabapentin Patents, Depomed has failed to demonstrate that Gralise is a commercial success, much less that any performance of the product can be attributed to the claimed invention of the '962 Patent. (FOF ¶¶ 247-254.) In addition to the reasons discussed above, the '962 Patent is only the subject of two of Depomed's licenses. (FOF ¶ 252.) The Abbott license, as explained above, is the antithesis of commercial success. (Id.) The second license, in addition to licensing the '962 Patent also licenses Depomed patents that are not at issue in this case including the '475 Patent and other "know-how." (FOF ¶ 251.) In situations such as this, where there are multiple patents covering a product, no presumption of nexus is appropriate, Therasense, 593 F.3d at 1299, and "a 'nexus must be established between the merits of the claimed invention

and evidence of commercial success before that evidence may become relevant to the issue of obviousness.'" Iron Grip Barbell, 392 F.3d at 1324 (citation omitted).

III. THE '280 PATENT IS INVALID FOR INDEFINITENESS

A. Claims that Fail to Inform with Reasonable Certainty are Invalid as Indefinite.

456. A patent specification must "conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the inventor or a joint inventor regards as the invention." 35 U.S.C. § 112, ¶ 2. "[A] patent is invalid for indefiniteness if its claims, read in light of the specification delineating the patent, and the prosecution history, fail to inform, with reasonable certainty, those skilled in the art about the scope of the invention." Nautilus, Inc. v. Biosig Instruments, Inc., --- U.S. ---, 2014 WL 2440536, at *2 (June 2, 2014). "[The] patent must be precise enough to afford clear notice of what is claimed, thereby apprising the public of what is still open to them." Id. at *5 (citation omitted); Amgen Inc. v. Hoechst Marion Roussel, Inc., 314 F.3d 1313, 1342 (Fed. Cir. 2003) (this assures that the claims are "sufficiently precise to permit a potential competitor to determine whether or not he is infringing"). The presumption of validity under 35 U.S.C. § 282 "does not alter the degree of clarity that § 112, ¶ 2 demands from patent applicants; to the contrary, it incorporates that definiteness requirement by reference." Nautilus, 2014 WL 2440536 at *6 n. 10. Anything less than demanding "reasonable certainty" would "leave courts and the patent bar at sea without a reliable compass." Id. at *6.

B. The Asserted Claims of the '280 Patent are Invalid as Indefinite for Failing to Inform with Reasonable Certainty.

457. Claims 1, 12, 14 and 45 of the '280 Patent are invalid as indefinite under 35 U.S.C. § 112, ¶ 2, because the claim limitation "is of a size exceeding the pyloric diameter in the fed mode" is not meaningfully precise. (FOF ¶¶ 274-280.) The pyloric diameter is highly

variable and that it is not possible to know what its size is in any given patient or at any given time. (FOF ¶ 277.) In fact, there is no specific size for improving gastric retention of a dosage form in the art given the uncertainty and variability between people. (Id.) When asked about weather specific sizes exceed the pyloric diameter, Dr. Annunziata, an expert in gastrointestinal physiology, was unable to do so. (Id.) This claim limitation, therefore, does not reasonably convey to one of ordinary skill in the art what swollen tablet dimensions are within the scope of the limitation "is of a size exceeding the pyloric diameter in the fed mode." Consequently, the asserted claims of the '280 Patent are indefinite because "its claims, read in light of the specification delineating the patent, and the prosecution history, fail to inform, with reasonable certainty, those skilled in the art about the scope of the invention." Nautilus, 2014 WL 2440536 at *2.

IV. ACTAVIS DOES NOT INFRINGE ANY ASSERTED CLAIMS OF THE PATENTS-IN-SUIT

458. Depomed must prove by a preponderance of the evidence that the Actavis ANDA Products meet each and every limitation of asserted claims. Glaxo, Inc. v. Novopharm, Ltd., 110 F.3d 1562, 1565 (Fed. Cir. 1997); Southwall Techs., Inc. v. Cardinal IG Co., 54 F.3d 1570, 1575 (Fed. Cir. 1995). That determination is a question of fact. Phonometrics, Inc. v. Westin Hotel Co., 319 F.3d 1328, 1331 (Fed. Cir. 2003). Where a patent contains both independent and dependent claims, "it is axiomatic that dependent claims cannot be found infringed unless the claims from which they depend have been found to be infringed." Minn. Mining & Mfg. Co. v. Chemque, Inc., 303 F.3d 1294, 1302 (Fed. Cir. 2002) (citation and internal quotation marks omitted).

459. Infringement can be direct or indirect. 5 Donald S. Chisum, Patents § 17.01. Direct infringement occurs where the accused infringer itself satisfies each and every limitation

of at least one independent claim. Id. at § 16.01. Indirect infringement occurs through active inducement or contributory infringement. Id. at § 17.01. Because pharmaceutical companies do not use or administer the drug, an ANDA filer will not directly infringe a method of using a drug. Alza Corp. v. Andrx Pharm., LLC, 607 F. Supp. 2d 614, 623 (D. Del. 2009) (citing Warner-Lambert Co. v. Apotex Corp., 316 F.3d 1348, 1363 (Fed. Cir. 2003)).

460. According to 35 U.S.C. § 271(b), "[w]hoever actively induces infringement of a patent shall be liable as an infringer." Infringement by inducement can only occur if there is direct infringement. Novartis Pharms. Corp. v. Eon Labs Mfg., 363 F.3d 1306, 1308 (Fed. Cir. 2004); S. Bravo Sys., Inc. v. Containment Techs. Corp., 96 F.3d 1372, 1376 (Fed. Cir. 1996).

461. Section 271(b) requires proof of intent to cause the acts that constitute infringement. Hewlett- Packard Co. v. Bausch & Lomb, 909 F.2d 1464, 1469 (Fed. Cir. 1990). "It must be established that the defendant possessed specific intent to encourage another's infringement and not merely that the defendant had knowledge of the acts alleged to constitute inducement." Manville Sales Corp. v. Paramount Sys., Inc., 917 F.2d 544, 553 (Fed. Cir. 1990). In other words, the plaintiff must show that the defendant knew or should have known that his actions would induce actual infringements. DSU Medical Corp. et al. v. JMS Co. Ltd., et al., 471 F.3d 1293, 1306 (Fed. Cir. 2006). "Accordingly, inducement requires evidence of culpable conduct, directed to encouraging another's infringement, not merely that the inducer had knowledge of the direct infringer's activities." Id. "A good-faith belief of invalidity is evidence that may negate the specific intent to encourage another's infringement, which is required for induced infringement." Commil USA, LLC v. Cisco Sys., Inc., 720 F.3d 1361, 1368 (Fed. Cir. 2013).

462. A company is liable for contributory infringement if it "offers to sell or sells within the United States or imports into the United States a component of a patented machine, manufacture, combination or composition, or a material or apparatus for use in practicing a patented process, constituting a material part of the invention, knowing the same to be especially made or especially adapted for use in an infringement of such patent." 35 U.S.C. § 271(c). In order to demonstrate contributory infringement, a patentee must show that an alleged contributory infringer "knew that the combination for which its components were especially made was both patented and infringing." Golden Blount, Inc. v. Robert H. Peterson Co., 365 F.3d 1054, 1061 (Fed. Cir. 2004). Contributory infringement does not arise when the article is a staple or commodity that has substantial, non-infringing uses. 35 U.S.C. § 271(c); Golden Blount, 365 F.3d at 1061.

463. Depomed has failed to meet its burden of proof in establishing Actavis' ANDA Products meet each and every limitation of asserted claims and has failed to meet its burden of establishing Actavis intends induce infringement of the asserted method claims.

A. Actavis' ANDA Products Do Not Infringe the Asserted Claims of the Gabapentin Patents.

1. Actavis' ANDA Products Do Not "Swell . . . in the Stomach" as Required by the Asserted Claims of the '927, '756 and '989 Patents.

464. All the asserted claims of the '927, '756, and '989 Patents require that the dosage form, when administered, "swells . . . in the stomach." (FOF ¶ 281.) This swelling is necessary to promote retention of the dosage form in the stomach. (Id.)

465. Depomed has failed to establish Actavis' ANDA Products swell to increase its size in the stomach. Without *in vivo* testing or a correlation between the *in vitro* testing that was done and the conditions that would be present in a fed stomach, Depomed cannot prove infringement.

466. [redacted]

467. [redacted] Depomed failed, however, to draw a link between the *in vitro* swelling studies and the conditions in the stomach in the fed mode and the impact these differences may have on swelling. (FOF ¶ 284.) For example, Dr. Annunziata testified that he could not say as a matter of reasonable scientific certainty whether Actavis' ANDA Tablets swell in the stomach to the same extent they would swell in the *in vitro* studies performed by Depomed and Actavis because the tablets would be subjected to more destructive forces in the stomach than in the *in vitro* tests. (Id.) Dr. Williams did not extrapolate the *in vitro* swelling data to *in vivo* data with food in the stomach nor did he conduct any investigation as to whether the dimensions of the tablets would be the same in a stomach as in a static model. (Id.) Drs. Felton and Derendorf both insisted that *in vitro* data does not replicate *in vivo* conditions time and time again. (Id.)

468. The more reasonable inference is that Actavis' tablets do not swell to the same extent in a stomach in the fed mode as the *in vitro* swelling studies would suggest. (FOF ¶ 285.) As Dr. Friend and Dr. Annunziata explained, the destructive forces in the stomach would act on the tablet just as much as they would on food particles. These destructive forces would tend to reduce the tablet's ability to swell. (FOF ¶ 283.) Swelling studies, therefore, have "little to no

relevance" standing alone as to whether and to what extent the tablet would swell in the stomach in the fed mode. (FOF ¶ 285.)

469. That Actavis' ANDA products are gastric retained does not mean that the tablets swell in the stomach, much less to a particular size. (FOF ¶ 286.) Dr. Annunziata explained that any particles over two to three millimeters in size can be gastric retained for a significant period of time. (Id.) Actavis' ANDA Products exceed this size without any swelling. (Id.) Dr. Annunziata also explained that tablets and other materials can be gastric retained even in the absence of swelling. (Id.) He explained that special camera-containing non-swelling capsules that are about 23 mm by 11 mm in diameter can be gastric retained for "an hour or two hours, three hours, sometimes even longer than that. (Id.)

470. Furthermore, in the EAG swelling studies, the technician performing the experiments noted that, during testing, Actavis' ANDA Products began floating in the simulated gastric fluid. (FOF ¶ 287.) Floating of the dosage form in the stomach would be an alternative way in which gastric retention is promoted, that is independent of and unrelated to any swelling of Actavis' ANDA Products that may occur.

471. Furthermore, Dr. Annunziata explained that when Actavis' ANDA Products are exposed to simulated gastric fluid, they get soft and sticky. (FOF ¶ 288.) He further explained that such sticky materials can adhere to the sides of the stomach and become gastric retained for that reason. (Id.) Again, gastric retention because of adherence would be independent of and unrelated to any swelling of Actavis' ANDA Products that may occur.

472. Thus, for these reasons, gastric retention is not a reliable indication that Actavis' ANDA Products swell in the stomach. (FOF ¶ 290.)

473. Depomed has therefore failed to establish Actavis' ANDA Products will "***swell*** . . . to promote gastric retention of the dosage form ***in the stomach***" as required by all of the asserted claims of the '927, '756 and '989 Patents. Thus, Actavis ANDA Products fail to meet each and every limitation and therefore do not infringe the asserted claims of the '927, '756 and '989 Patents. Glaxo, 110 F.3d at 1565; Southwall, 54 F.3d at 1575.

2. Actavis' ANDA Products Do Not Contributorily Infringe or Induce Infringement of the Method of Treatment Claims in the '927, '756, '332 and '992 Patents.

474. Depomed has not established that Actavis induces or contributes to the infringement of claims 18, 25, 26, 34, 61 and 62 of the '927 Patent, claims 6, 7 and 11 of the '756 Patent, claims 12, 22, 24 of the '332 Patent and claim 22 of the '992 Patent (collectively, the "Method Claims").

475. With respect to the asserted claims of the '927 and '756 Patents, as described above, Depomed has failed to prove that Actavis' ANDA Products will "swell . . . in the stomach," as required by the claims. In the absence of a direct infringement of the claims of the '927 and '756 Patents, there can be no indirect infringement. Novartis Pharms. Corp., 363 F.3d at 1308; S. Bravo Sys., Inc., 96 F.3d at 1376.

476. As a pharmaceutical company, Actavis does not directly administer drugs to patients and therefore does not directly infringe the Method Claims. Alza Corp., 607 F. Supp. 2d at 623 (citing Warner-Lambert, 316 F.3d at 1363).

477. To establish induced infringement, Depomed has the burden to establish that Actavis knew or should have known that its actions would induce actual infringements. DSU Medical Corp., 471 F.3d at 1306. Depomed has adduced no evidence from Actavis' current and former employees regarding any specific intent to infringe any of the asserted patents. (FOF ¶ 295.) Additionally, "[a] good-faith belief of invalidity is evidence that may

negate the specific intent to encourage another's infringement, which is required for induced infringement." Commil USA, LLC v. Cisco Sys., Inc., 720 F.3d 1361, 1368 (Fed. Cir. 2013). By virtue of this action it is clear Actavis believes Depomed's patents to be invalid. Thus, Depomed has failed to establish Actavis' ANDA Products induce infringement of the Method Claims.

478. In order to demonstrate contributory infringement, a patentee must show that an alleged contributory infringer "knew that the combination for which its components were especially made was both patented and infringing." Golden Blount, Inc., 365 F.3d at 1061. Contributory infringement does not arise when the article is a staple or commodity that has substantial, non-infringing uses. 35 U.S.C. § 271(c); Golden Blount, 365 F.3d at 1061.

479. Depomed has failed to demonstrate that Actavis intends to contributorily infringe the Method Claims. [redacted] Thus, Depomed has failed to establish Actavis' ANDA Products contributorily infringe the Method Claims.

480. Furthermore, Depomed is barred from arguing that Actavis' ANDA Products infringe the Method Claims of the '927, '756, '332 and '992 Patents because Depomed provided no evidence or expert opinions regarding infringement under the doctrine of equivalents.

B. Actavis' 600 mg Product Does Not Infringe the Asserted Claims of the '962 Patent – The Oval Patent.

481. Claims 5, 8, 10 and 13 of the '962 Patent all require that the dosage form have "a shape which when projected onto a plane, is either an oval or a parallelogram." (FOF ¶ 133.)

Depomed admits that Actavis' 300 mg ANDA Product does not infringe the '962 Patent. (FOF ¶ 299.) Depomed does not contend that Actavis' 600 mg ANDA Product is in the shape of a parallelogram. (FOF ¶ 300.) Depomed has not established that that Actavis' 600 mg ANDA Product is in the shape of an oval. (FOF ¶ 307.) Thus, Depomed has not established that that Actavis' 600 mg ANDA Product infringes the asserted claims of the '962 Patent.

482. Depomed's expert, Dr. Hopfenberg, admits that the '962 Patent discloses a great number of different shapes to promote gastric retention, but only claims oval and parallelogram. (FOF ¶ 301.) Dr. Hopfenberg explained that these are recognized in the art to be distinct shapes. (Id.) The '962 Patent also criticizes "tablet or caplets (cylindrical tablets with rounded ends) that are elongated in shape to facilitate swallowing." (Id.) The '962 Patent explains that these may orient in the vicinity of the pylorus such that their longest dimension is in alignment with the pyloric axis, and therefore pass through the pylorus without being gastric retained. (Id.) Thus, Depomed disclaimed and dedicated to the public other shapes such as triangle, almond, peanut, 'bow tie,' trapezoidal, pentagonal, and hexagonal, as well as elongated tablet and caplet shapes. Sage Products, Inc. v. Devon Industries, Inc., 126 F.3d 1424, 1425 (Fed. Cir. 1997) ("[A]s between the patentee who had a clear opportunity to negotiate broader claims but did not do so, and the public at large, it is the patentee who must bear the cost of its failure to seek protection for this foreseeable alteration of its claimed structure."); Phillips v. AWH Corp., 415 F.3d 1303, 1312 (Fed. Cir. 2005) ("It is a bedrock principle of patent law that "the claims of a patent define the invention to which the patentee is entitled the right to exclude.")

483. Depomed's disclaimer of these other shapes also makes clear that the term "oval" should be applied narrowly so as to not encompass shapes that Depomed distinguished and disclaimed such as elongated tablet and caplet shapes, almond shapes and the like. SciMed Life

Sys., Inc. v. Advanced Cardiovascular Sys., Inc., 242 F.3d 1337, 1345 (Fed. Cir. 2001) (holding that a particular structure is "deemed outside the reach of the doctrine of equivalents because that structure is clearly excluded from the claims whether the exclusion is express or implied.").

484. With respect to the phrase "a first and second orthogonal axes of unequal length" in the claim construction of the term "oval," during trial Dr. Hopfenberg argued that the "axes" must be planes of symmetry, relying on extrinsic dictionary definitions. (5/14/2014 Tr. 443:3-22, 493:3-21.) Applying this definition, Dr. Hopfenberg stated that other shapes, such as almond, that are disclosed in the specification as being a possible shape for the dosage form only have "only one axis," and thus were distinguishable. (Id. at 482:11-17, 491:20-492:9; JTX 1 at col. 4, ll. 7-22.)

485. Dr. Hopfenberg's attempt to redefine the claim construction, however, finds no support in the '962 Patent's intrinsic evidence. Phillips, 415 F.3d at 1313-15 (the specification is "the single best guide to the meaning of a disputed term") (citations omitted). The '962 Patent does not explicitly define the term "axis." The '962 Patent specification states, however, that "[s]ome of the possible shapes" for the dosage form "are oval, triangle[and] almond . . . provided (as stated above) that the largest planar projection of the shape has ***at least two orthogonal dimensions***, one being larger than the other." (JTX 1 at col. 4, ll. 10-15 (emphasis added).) The specification then provides that the two "[p]referred shapes are oval and parallelogram." (JTX 1 at col. 4, ll. 15-22.) Thus, in describing the shapes, the '962 Patent defined the shapes that promote gastric retention to be those with ***two orthogonal dimensions*** of unequal length, thereby not requiring the symmetry as Dr. Hopfenberg seeks to interject. (Id.) Although Depomed points to the phrase "[p]articularly preferred shapes are those that have three (orthogonal) planes of ***symmetry***" (id. at col. 4, ll. 15-22 (emphasis added); 5/14/2014

Tr. 542:10-17) to suggest that axes define a plane of symmetry, an oval does not have three planes of symmetry. Thus, this phrase that speaks to "[p]articularly preferred shapes" is irrelevant to the construction of the term "oval." The intrinsic evidence is thus dispositive – the phrase "axes of unequal length" is synonymous with the "two orthogonal dimensions of unequal length" described in the specification, as that was that was the specification stated is characteristic of the "possible" shapes of the '962 Patent dosage forms. (JTX 1 at col. 4, ll. 10-15, claim 1.) Phillips, 415 F.3d at 1315-16 (the specification is usually "dispositive"). Furthermore, as Dr. Friend explained, one of ordinary skill in the art of pharmaceutical formulation would not understand the term "axis" in the '962 Patent to require symmetry. (5/14/2014 Tr. 505:23-506:2, 506:8-507:10.)

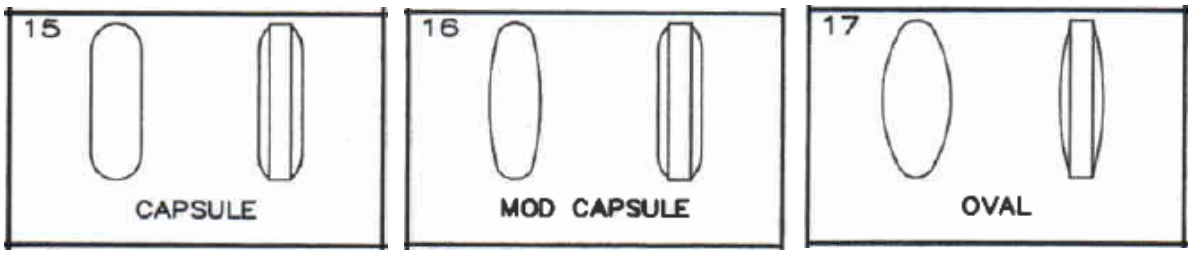
486. Dr. Hopfenberg also found a requirement of symmetry in the dictionary definition of "axis" to support his argument. (Id. at 493:3-21.) As an initial matter, an extrinsic dictionary definition cannot be used to contradict the clear guidance of the specification. Phillips, 415 F.3d at 1322-23 (a dictionary may be used "when construing claim terms, so long as the dictionary definition does not contradict any definition found in or ascertained by a reading of the patent documents"). Furthermore, the dictionary definitions on which he relied merely stated that an axis often defines a plane of symmetry but it is not a mandatory requirement. (5/14/2014 Tr. 493:3-494:5 (the main dictionary definition of axis was "a straight line about which a body or geometric object rotates or may be thought to rotate" and the second definition given was "an[] unlimited line, half line or line segment serving to orient a space or geometric object" that finished with "especially a line about which the object is symmetrical," preferring but not make symmetry a requirement).) The dictionary definitions and the '962 Patent specification both

support what Dr. Friend explained – that one of ordinary skill in that art would not define orthogonal axis as requiring symmetry. (Id. at 506:11-507:10.)

487. [redacted]

488. There are a limited number of shapes that are commonly used in manufacturing pharmaceutical tablets. (FOF ¶ 304.) Dr. Friend points to a TABLETING SPECIFICATION MANUAL that describes about 25 such shapes. (Id.) Dr. Hopfenberg testified regarding a TABLET DESIGN TRAINING MANUAL from the Elizabeth Carbide Die Company that contains a table showing similar tablet shapes. (Id.)

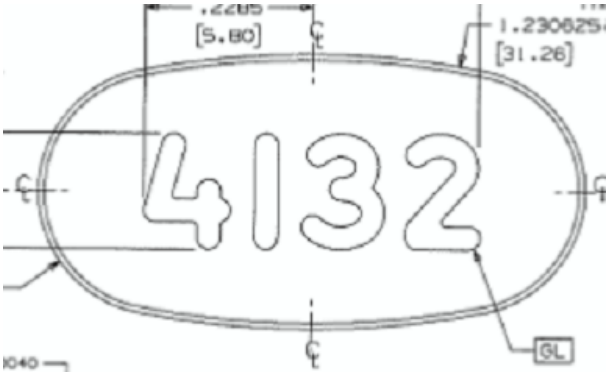
489. The American Pharmacists Association, in their TABLETING SPECIFICATION MANUAL, clearly differentiates an oval from a modified capsule, which is the shape of Actavis' 600 mg tablet. (FOF ¶ 305.)



(Id.) Dr. Friend explained that these are distinct shapes in the pharmaceutical arts. (Id.) He explained that "the primary difference between the capsule and modified capsule is the slight widening towards the center of the tablet," but that the two "look very similar." (Id.) In contrast,

the oval is a continuous curve along the side as opposed to the disjointed curves that create the slight widening seen on the side of the modified capsule. (Id.) Dr. Hopfenberg similarly testified, based on the ENCYCLOPEDIA OF PHARMACEUTICAL TECHNOLOGY, that oval tablet shapes are distinct from capsule and modified capsule tablet shapes (as well as other shapes like almond shapes, peanuts, and bow tie shapes). (Id.)

490. The curvature of Actavis' 600 mg ANDA Product is not as pronounced as the oval shapes depicted in the TABLETING SPECIFICATION MANUAL or the ENCYCLOPEDIA OF PHARMACEUTICAL TECHNOLOGY relied upon by the experts in this case. (FOF ¶ 306.) For example, the drawing for the punches used to make the tablets show the following profile for the tablets:



(Id.) [redacted]

[redacted]

[redacted]

491. Thus, Actavis' 600 mg ANDA Product does not meet the claim limitation "a shape which when projected onto a plane, is either an oval or a parallelogram," and thus does not infringe the asserted claims of the '962 Patent. Thus, Actavis ANDA Products fail meet each and every limitation and therefore do not infringe the asserted claims of the '962 Patent. Glaxo, 110 F.3d at 1565; Southwall, 54 F.3d at 1575.

492. Furthermore, Depomed is barred from arguing that Actavis' ANDA Products infringe the asserted claims of the '962 Patent for the following three reasons: (1) Depomed provided no evidence or expert opinions regarding infringement under the doctrine of equivalents; (2) the "oval" limitation was added by amendment during prosecution and equivalents are thus barred by prosecution history estoppel; and (3) the capsule shape of Actavis 600 mg Product was disclaimed in the '962 Patent specification as being problematic.

493. Depomed amended the claims to limit the shapes of the tablet to an "oval or parallelogram" during prosecution of the '962 Patent to overcome the examiner's rejection of the pending claims in view of the prior art. (FOF ¶ 302.) As such, equivalents to this limitation are barred by the doctrine of prosecution history estoppel. Biagro Western Sales, Inc. v. Grow More, Inc., 423 F.3d 1296, 1306-07 (Fed. Cir. 2005) (prosecution history barred equivalents notwithstanding patentee's argument that amendment was not relied upon and was unnecessary for patentability); Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co., 535 U.S. 722, 724

(2002); Honeywell Int'l, Inc. v. Hamilton Sundstrand Corp., 370 F.3d 1131, 1139 (Fed. Cir. 2004).

494. In the specification of the '962 Patent, Depomed criticized capsule shaped and other elongated tablet shapes as having a shape that is unfavorable for gastric retention. In particular, the specification states that "[e]ven with swelling . . . particles can pass through the pylorus . . . if the particles become oriented . . . such that their longest dimension is in alignment with the pyloric axis. This is particularly true of tablets or caplets (cylindrical tablets with rounded ends) that are elongated in shape to facilitate swallowing." (JTX 1, col. 3, ll. 1-20.) Depomed cannot reclaim through the doctrine of equivalents such shapes that were clearly criticized and disclaimed in the specification. See SciMed Life Sys., Inc. v. Advanced Cardiovascular Sys., Inc., 242 F.3d 1337, 1345 (Fed. Cir. 2001) (holding that a particular structure is "deemed outside the reach of the doctrine of equivalents because that structure is clearly excluded from the claims whether the exclusion is express or implied.").

C. Actavis' ANDA Products Do Not Infringe the Asserted Claims of the '280 Patent – The Platform Patent.

495. All the asserted Claims of the '280 Patent require that the dosage form swell to "a size exceeding the pyloric diameter in the fed mode to promote retention in the stomach during said fed mode." (FOF ¶ 309.) Depomed has not established that the Actavis ANDA Products swell to exceed the pyloric diameter in the fed mode for two reasons: (1) Depomed is not able to establish a correlation between its *in vitro* testing and the size of Actavis' tablet *in vivo*; and (2) the evidence demonstrates that the size of the pyloric diameter is highly variable to the extent that Depomed cannot establish the Actavis ANDA Products attained a size exceeding the pyloric diameter when swollen.

496. The pyloric diameter here refers to the diameter of the pylorus during the brief periods of relaxation when larger materials can escape the stomach, and not the periods of time during which the pylorus is clenched tightly closed to prevent the stomach contents from being expelled into the intestines. (Id.)

497. As an initial matter, Dr. Annunziata admitted that particles that are smaller than the diameter of the relaxed pylorus in the fed mode can still be retained in the stomach during the fed mode. (FOF ¶ 310.) Thus, evidence of gastric retention is not probative of the size of Actavis' ANDA Products when in the fed stomach. (Id.)

498. As explained above, Depomed has failed to demonstrate that Actavis' ANDA Products swell in the stomach in the fed mode, much less to a particular size exceeding the pyloric diameter. For this reason alone, Depomed has failed to prove infringement.

499. But even if Depomed's evidence of swelling is accepted, Depomed has failed to demonstrate that the swollen dimensions of Actavis' ANDA Products exceed the size of the pyloric diameter in the fed mode.

500. As Dr. Annunziata admitted, the pyloric diameter is "definitely variable as everybody, every person is variable, in size, shape, et cetera" and so he could not say with reasonable scientific certainty whether 12 millimeters or even 20 millimeters exceeds the size of the pyloric diameter. (FOF ¶ 311.) In Braintree Laboratories, Inc. v. Novel Laboratories, Inc., the Federal Circuit held that, to show infringement of a patent claiming an effect in "a patient," the patentee must show evidence that the accused product had that effect in "the general class of persons to whom the patented compositions are directed, i.e., a patient population." No. 2013-1438, --- F.3d ---, 2014 WL 1584451, at *7 (Fed. Cir. Apr. 22, 2014). Depomed has not shown

that the Actavis ANDA Products are "of a size exceeding the pyloric diameter" in the population to whom the patented compositions are directed and thus fails to prove infringement.

501. [redacted]

502. [redacted]

503. Depomed has failed to establish that Actavis' ANDA Products meet each and every limitation of the asserted claims of the '280 Patent, and therefore Depomed has failed to establish that Actavis' ANDA Products infringe the asserted claims of the '280 Patent. Glaxo, 110 F.3d at 1565; Southwall, 54 F.3d at 1575.

504. Furthermore, Depomed provided no evidence or expert opinions regarding infringement under the doctrine of equivalents. In any event, Depomed is barred from asserting the doctrine of equivalents because the limitation "a size exceeding the pyloric diameter in the fed mode" was added by amendment for purposes of patentability. (See, *supra*, ¶ 23.) Biagro Western Sales, Inc., 423 F.3d at 1306-07.

Respectfully submitted,

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